CE 2.5 ANCC Contact Hours

Complex Care: Ventilation Management When Brain Injury and Acute Lung Injury Coexist

Jacqueline Modock

ABSTRACT

The purpose of this article is to explore the management of coexisting brain insult and acute lung injury to help guide clinicians in balancing what may appear to be competing goals. First, contemporary management of mechanically ventilated patients with either brain or lung injury diagnoses is reviewed, followed by a review of intracranial pressure and acute lung injury/acute respiratory distress syndrome. The article ends with a discussion of a literature review regarding possible treatment balance when the two conditions coexist.

Keywords: acute lung injury, acute respiratory distress syndrome, brain insult, stroke, subarachnoid hemorrhage, traumatic brain injury, ventilator management

The Centers for Disease Control and Prevention (Faul, Xu, Wald, & Coronado, 2010) report that 1.7 million people experience traumatic brain injury (TBI) annually. Reports indicate that 2%–51% of people with TBI require intubation (Dunham et al., 2003). Although the initial traumatic insult can lead to damage of the lung (i.e., contusion or rib fractures), many of these patients develop acute lung injury (ALI) unrelated to the initial traumatic insult. Whether the patient presents with TBI, subarachnoid hemorrhage, or ischemic stroke, several possible contributing factors can lead to the development of ALI. Some of the identified contributing factors include neurogenic pulmonary edema, aspiration, shock, crystalloid administration, induced arterial hypertension, or systemic inflammatory reaction (Contant, Valadka, Gopinath, Hannay, & Robertson, 2001; Eberhard et al., 2000; Holland et al., 2003; Mascia, 2009). The management of a patient with a brain injury who develops ALI is challenging because of conflicting goals for the control of carbon dioxide levels in the two disease processes. The challenge facing the clinician in this situation is how to preserve optimal oxygenation in the lungs while protecting the damaged and vulnerable brain. This article highlights the issues clinicians face while trying to preserve optimal cerebral blood flow and protect the lungs in brain-injured patients with ALI or acute respiratory distress syndrome (ARDS). The purpose of this article is to explore the management of coexisting brain insult and ALI, including emerging data from animal models, to guide the clinician in balancing what may appear to be competing goals. First, contemporary management of mechanically ventilated patients with either brain or lung injury diagnoses is reviewed, followed by a review of intracranial pressure (ICP) and ALI/ARDS. The article concludes with a discussion of a literature review regarding possible treatment balance when the two conditions coexist.

Current Management Guidelines

The Guidelines for the Management of Severe Traumatic Brain Injury (Brain Trauma Foundation, 2007) contains recommendations for oxygenation targets. Surprisingly, the recommendation provides level III evidence concerning hypoxemia in the brain-injured patient because insufficient data are available to support a higher recommendation. The current recommendation is simply that hypoxia should be avoided (PaO_2 < 60 mm Hg or O_2 saturation < 90%). Recommendations on carbon dioxide levels for the brain-injured patient are to maintain normocapnia between 35 and 40 mm Hg. Hyperventilation as a temporizing measure to treat elevated intracranial hypertension is a level III recommendation (Brain Trauma Foundation, 2007).

Guidelines for the management of ALI and the more severe ARDS center around reduced tidal volumes (6 ml/kg) and lower plateau pressures (<30 cm H_2O) to increase oxygenation (Ventilation with lower tidal, 2000). A potential consequence of this mode of ventilation is the development of hypercapnia because of insufficient exchange of carbon dioxide due to the lower tidal volumes. Hypercapnia is usually tolerated by patients with ALI/ARDS but becomes more problematic with the concurrent diagnosis of brain injury.

Questions or comments about this article may be directed to Jacqueline Modock, MSN BSN, at Jmm286@case.edu. She is an AGACNP at Lake Tahoe Regional Hospital, Reno, NV.

The author declares no conflicts of interest.

DOI: 10.1097/JNN.0000000000000042

Exploring the Role of Carbon Dioxide in ICP and ALI/ARDS

Regardless of the type of brain injury experienced by a patient, a major goal of the clinician is to maintain normal cerebral perfusion pressure (CPP) and ICP to provide the injured brain with optimal oxygenation. The importance of managing CPP in the brain-injured patient is amplified when autoregulation is impaired. The clinician needs to recognize decrements in CPP and provide treatment quickly to maintain safe and effective levels of perfusion to the brain (Rangel-Castilla, Gopinath, & Robertson, 2008). The challenge in brain-injured patients is often the dramatic increases in ICP that lead to intracranial hypertension and decreased CPP. Intracranial hypertension can be caused by multiple sources. There can be an intracranial cause such as a brain tumor; trauma; intracerebral hemorrhage; hydrocephalus; and/or extracranial causes such as hypoxia, hypercarbia, posture, hyperpyrexia, seizures, or drugs (Rangel-Castilla et al., 2008). The mechanisms by which each of the different causes of intracranial hypertension affects ICP are diverse. Hypercarbia's physiological explanation is that carbon dioxide combines with water in body fluids to form carbonic acid. The carbonic acid dissociates to form hydrogen ions that cause vasodilation of the cerebral vessels and cerebral volume expansion (Hall, 2011).

Clinicians have used hyperventilation as a means to lower carbon dioxide in the blood, causing vasoconstriction of the cerebral vessels to lower ICP. Hyperventilation may be temporary, to reverse a transient increase in ICP, or sustained, such as with mechanical ventilation strategies of increased tidal volume or respiratory rate to achieve an arterial carbon dioxide level of 32–34 mm Hg for persistent elevated ICP. Currently, this intervention is controversial and applied in the emergent treatment of intracranial hypertension (Brain Trauma Foundation, 2007; Rangel-Castilla et al., 2008).

ALI and ARDS are distinct diagnoses with treatment guidelines specific to the diseases. The ARDS consensus statement (Bernard et al., 1994) defines ALI and ARDS as two individual syndromes. The criteria for ALI are the following:

- Acute onset
- PaO_2/FiO_2 ratio ≤ 300 mm Hg
- Bilateral infiltrates on chest radiograph
- Pulmonary artery wedge pressure ≤ 18 mm Hg or no clinical evidence of left arterial hypertension

The criteria for ARDS include all those of ALI except for the PaO_2/FiO_2 ratio of ≤200 mm Hg (Bernard et al., 1994). The pathophysiology of ALI/ARDS involves several stages and pathways. The beginning exudative stage with diffuse alveolar damage and pulmonary edema is followed by the proliferative phase in which interstitial and alveolar inflammation, fibrosis, and disordered healing occur (Lanken, 2005). The result of these cellular changes is reduced lung compliance and severe hypoxia (Lanken, 2005). Although there is believed to be many precipitating causes to developing ALI/ARDS, such as aspiration, pneumonia, sepsis, and others, all these causes follow a ''final common pathway'' that leads to lung tissue damage (Lanken, 2005).

Historically, treatment of hypoxemia in patients with ALI/ARDS involved applying positive end-expiratory pressure (PEEP) and using large tidal volumes (10–15 ml/kg) that led to higher peak and end-inspiratory pressures (Lanken, 2005). The ultimate goals of this approach were to maintain arterial oxygen saturations (PaO_2) above 88%–90% and keep arterial pH and carbon dioxide ($PaCO_2$) within normal limits (Brower, 2002; Lanken, 2005). Then in 2000, a multicenter, randomized study conducted by the Acute Respiratory Distress Syndrome Network challenged the traditional ventilator management approach and found that ventilation with lower tidal volumes (6 ml/kg) and decreased peak pressures (30 cm H_2O or less) resulted in decreased mortality for the treatment group (Ventilation with lower tidal, 2000). Treatment goals for ALI/ARDS then shifted to a lung protective strategy that no longer focused on maintaining arterial pH and $PaCO_2$ within normal limits but rather allowed for permissive hypercapnia (Brower, 2002; Lanken, 2005; Ventilation with lower tidal, 2000).

> Ongoing management of cerebral perfusion pressure (CPP) is critical in all brain-injured patients but is significantly more challenging in patients with acute lung injuries who must be supported with mechanical ventilation.

Coexistence of Brain Injury and ALI/ARDS

A retrospective study conducted to look at the prevalence of ALI/ARDS in traumatic brain-injured patients found that the prevalence of ALI/ARDS increased from 2% in 1988 to 22% in 2008 (Rincon et al., 2012).

Although the increased prevalence may be because of better definitions (the publication of the ARDS consensus statement in 1994), the 28% mortality associated with ALI/ARDS after a TBI remains significant and relatively unchanged from 1988 (Rincon et al., 2012). The exact mechanism for the development of pulmonary dysfunction in brain-injured patients is unclear. Historically, the blast injury theory was one explanation as to why brain-injured patients developed neurogenic pulmonary edema (Theodore & Robin, 1975). This theory proposes that the sympathetic storm caused by elevations in ICP changes the intravascular pressure leading to endothelium damage and the escape of plasma into the alveoli (Mascia, 2009). Recently a Double Hit Model has been developed to explain why pulmonary dysfunction is often seen in brain-injured patients. This model states that a systemic inflammatory environment is created by the initial insult to the brain. This initial hit includes a catecholamine storm and inflammatory reactions. This then primes the body to be more vulnerable to secondary insults such as infections, lung trauma from mechanical ventilation, and transfusions (Mascia, 2009). Alternatively, ALI and ARDS can occur in the brain-injured patient because of primary lung damage (including preexisting disease), infection such as ventilator-associated pneumonia, and fluid therapy.

Recent research suggests that the options available to the clinician in balancing competing goals for carbon dioxide management are not as limited as once thought and that some ventilation strategies might improve lung function while preserving brain tissue.

PEEP

The use of PEEP has been well studied in both brain-injured patients and patients with ARDS. In ARDS, the alveoli collapse and become fluid filled. When PEEP is applied, partially collapsed alveoli are stented opened and recruited to provide improved oxygenation. However, PEEP also increases intrathoracic pressure with the potential to increase resistance to passive cerebral venous blood flow and cerebral spinal fluid outflow. Several studies have examined the effect of PEEP in brain-injured patients. Concerns over the effect of PEEP on ICP and CPP have been evaluated in several research studies. These studies support the practice of maintaining the PEEP below the patients' ICP (McGuire, Crossley, Richards, & Wong, 1997) and maintaining the mean arterial pressure at normal levels with either fluid or vasoactive drugs (Georgiadis, Schwarz, Baumgartner, Veltkamp, & Schwab, 2001; Muench et al., 2005). A study performed by Mascia (2009) further evaluated the effect of PEEP on ICP in patients with ALI brain injury. Those patients found not to respond as recruiters to increased levels of PEEP experienced increases in $PaCO_2$ secondary to hyperinflation of the lungs that lead to a significant increase in ICP mediated by cerebral vasodilation (Mascia, 2009). In those patients found to be recruiters after higher application of PEEP, there was no change in ICP but an improvement in oxygen saturation. Furthermore, researchers have found that PEEP can positively influence the brain tissue oxygen pressure in patients with brain injury and ALI (Nemer et al., 2011). Researchers have shown that PEEP can lead to an improvement in oxygen saturation but can also affect CPP by way of hypercapnia, vasodilation, and alterations in mean arterial pressure. Although PEEP may be a potentially effective method of increasing oxygenation, its application requires careful selection and continuous invasive monitoring of patients.

Tracheal Gas Insufflation

Tracheal gas insufflation offers the potential to balance low tidal volumes with normocapnia. In this treatment, a catheter is placed above the carina, and a set flow of gas is introduced during the expiratory phase of positive pressure ventilation. The result is a reduction in anatomic dead space and carbon dioxide in the airways (Ravenscraft et al., 1993). There is limited data related to the use of this therapy in brain-injured patients. One prospective study of seven patients with severe head trauma and ALI/ARDS found that tracheal gas insufflation resulted in decreased tidal volumes (from 9.1 to 7.2 ml/kg) while maintaining normocapnia (i.e., $PaCO_2$ of 35–40 mm Hg; Martinez-Perez et al., 2004). Other results included slight improvement in oxygenation and no significant changes in ICP (Martinez-Perez et al., 2004). These findings are consistent with outcomes from an earlier case report (Levy, Bollaert, Nace, & Larcan, 1995). Although promising results, there are significant risks associated with the use of tracheal gas insufflation. This adjunctive treatment can cause an increase in auto-PEEP related to increased expiratory flow resistance, which can result in increased intrathorasic pressure and changes in ICP (Martinez-Perez et al., 2004). Other potential complications include tracheal erosion, oxygen toxicity, blood clot formation, and mucous and bronchial damage (Lanken, 2005; Levy et al., 1995). This intervention requires continuous monitoring and the use of additional specialized equipment. The lack of higher quality evidence regarding tracheal gas insufflation in brain-injured patients requires cautious use of this intervention. Use should be limited to those centers with experience in its use in patients with ARDS and to clinical trials.

High-Frequency Oscillatory Ventilation

The neonatal intensive care unit (ICU) introduced high-frequency oscillatory ventilation (HFOV) in the 1960s. Over the past decade, it has been identified as a type of rescue therapy for adults with ARDS. This mode of ventilation provides small tidal volumes and high mean airway pressures that prevent both collapse and overdistention of the alveoli, a key goal in ARDS treatment (Chan, Stewart, & Mehta, 2007). Concern with using HFOV in a brain-injured patient centers around changes in the partial pressure of carbon dioxide in the blood and blood pressure changes that ultimately may affect ICP and CPP (Young & Andrews, 2011). Several studies have explored the effects of HFOV in patients with brain injuries and ALI. Unfortunately, most human data collection has been conducted in small retrospective case series (Bennett, Graffagnino, Borel, & James, 2007; David et al., 2005). The only prospective trials researching HFOV to treat ALI with brain injury were conducted in animal models (David et al., 2006; Heuer et al., 2011). Interestingly, these data do provide limited support that HFOV may be an effective ventilation strategy in this patient population. When evaluating the effect of HFOV on cerebral hemodynamics, no study found uncontrollable changes in ICP or CPP during HFOV (Bennett et al., 2007; David et al., 2005). A single systematic review of limited data concluded that the current evidence ''should at best be considered as hypothesis generating rather than for drawing evidence-based conclusions'' (Young & Andrews, 2011). Although this review was unable to draw any conclusions about a mortality benefit in this subpopulation of patients with ALI and TBI, larger studies about ALI/ARDS have failed to show a mortality benefit with this mode of ventilation compared with traditional modes (Wunsch & Mapstone, 2004; Wunsch, Mapstone, & Takala, 2005; Young & Andrews, 2011). Ultimately, this mode of ventilation may be unrealistic for hospitals that do not have access to this specialized equipment. Furthermore, currently, no data provide strong support for its routine use. In those institutions with access to this mode of ventilation, use must be limited to patients with continuous invasive monitoring equipment including ICP, mean arterial pressure, $PaCO_2$, and SpO_2 and specially trained providers that can respond quickly to changing patient hemodynamics and only after thorough conversations with patient's family members.

Nitric Oxide

As a potent dilator of the pulmonary blood vessels, nitric oxide (NO) has been shown to improve oxygenation in patients with ARDS (Afshari, Brok, Moller, & Wetterslev, 2011). Several case reports have shown a rapid correction of hypoxemia and improvement in ICP after the administration of NO in brain-injured patients with ALI (Gritti et al., 2012; Papadimos, Medhkour, & Yermal, 2009; Vanhoonacker, Roeseler, & Hantson, 2012). These case reports have only included data for three patients between 20 and 37 years. All patients were successfully weaned from mechanical ventilation and experienced no complications related to NO use, but two patients continued to experience severe cognitive deficits after discharge (Papadimos et al., 2009; Vanhoonacker et al., 2012). Several interesting hypothesizes have been generated to explain the potential beneficial effect of NO, not only locally in the lungs but also distally with hippocampal preservation and influences on inflammation in TBI patients with ARDS (Papadimos et al., 2009). Drawing from previous research in ARDS and NO, NO has the potential to harm the kidneys and the risk of methemoglobin, in addition to a tremendous economic cost (Afshari et al., 2011; Lanken, 2005). A recently completed systematic review that included both adults and children found no significant effect on mortality, duration of ventilation, ventilator-free days, or length of ICU stay (Afshari et al., 2011). Whereas researchers continue to investigate the molecular interaction of NO in these patients and conduct randomized studies with large populations, the clinician remains without strong evidence to support the routine use of NO. Therefore, the utility of NO needs further investigation in brain- and lung-injured patients, and its routine use cannot be recommended at this time.

Prostacyclin Infusion

As a member of the prostaglandin family, prostacyclin is released by endothelial cells causing vasodilation and inhibition of platelets (Lowson, 2002). Inhaled and intravenous prostacyclin (PGI_2) have been used in pulmonary hypertension, ARDS, and peripheral vascular disease because of its vasodilatory properties and its interesting ability to stimulate NO production (Lowson, 2002). In addition, research has also shown a potential benefit of prostacyclin in reducing neuronal cell death after a brain injury (Bentzer, Mattiasson, McIntosh, Wieloch, & Grande, 2001). Researchers have also shown an improvement in lactate levels around the injured part of the brain, increased glucose, and improved jugular bulb blood oxygenation with low-dose (below those recommended for ARDS) prostacyclin administration (Grande, Moller, Nordstrom, & Ungerstedt, 2000). Potential adverse effects with its use include hypotension and bleeding owing to its vasodilating and platelet inhibiting properties. There has only been one case report of a single patient published in the literature regarding prostacyclin use in patients with TBI

and ALI/ARDS. Although the authors noted an improvement in brain tissue oxygenation, there was a slight increase in ICP without a significant effect on CPP (≥60 mm Hg) during prostacyclin initiation (Stiefel, Zaghloul, Bloom, Gracias, & LeRoux, 2007). After discontinuation of prostacyclin, the patient experienced an elevation in ICP, evolution of the contusion, and cerebral edema requiring a hemicraniectomy. Although no direct causation can be drawn from this event, this finding must raise serious concerns with prostacyclin use. This case report did use higher doses than those used in the prior mentioned trials that did not report any hemorrhagic complications. Until further research is conducted that examines the safety of prostacyclin in this subgroup of patients, the potential risks seem to outweigh the benefits and use cannot be recommended outside of controlled trials with informed patient/family consent.

Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation (ECMO) has recently been investigated in the treatment of brain-injured patients with ARDS (Lanken, 2005). ECMO can reduce hypercarbia, improve oxygenation, and allow the injured lung to rest or recover. The use of ECMO involves either veno-arterial or veno-venous cannulation of the femoral or jugular vessels. Complications include neurological injury, sepsis related to catheters, bleeding related to heparin administration, pneumothorax, oliguria, and cardiovascular and gastrointestinal complications (Mateen et al., 2011; Rodriguez, 2013). Most importantly, the clinician using ECMO must have special resources (i.e., ECMO devices, trained staff, and ability to provide sustained 1:1 or 2:1 care) and collaborate closely with cardiothoracic colleagues to provide this treatment option. Until recently, the mortality benefit of ECMO was questioned, but new research may be offering new insights into the potential benefit ECMO offers patients (Australia and New Zealand Extracorporeal Membrane Oxygenation Influenza Investigators et al., 2009; Peek et al., 2009). Only two reports have been published examining ECMO in brain-injured patients with ALI/ARDS. The first retrospective analysis examined five patients with TBI and ARDS who were connected to a pumpless extracorporeal lung assist system. The results were reductions in ICP and hypercapnia and improvement in oxygenation for three patients (Bein, Scherer, Philipp, Weber, & Woertgen, 2005). An additional case report documented the use of two oxygenators during ECMO in a patient with TBI and ARDS. The ECMO resulted in reduced CO_2 and improved oxygen saturation. After 7 days on ECMO and additional days of ICU and hospital care, the patient was discharged with normal neurological status (Leloup, Roze, Calderon, & Ouattara, 2011). These two small studies may highlight a potentially beneficial intervention for these patients. Additional study of the patient with both brain and lung injury and ECMO as an intervention is needed. Especially important is additional information about optimal sites for cannulation, effects of heparin administration, and neurological outcomes.

Hypercapnia

Perhaps, the most intriguing research challenges historical dogma about the effect of carbon dioxide on the injured brain. In a randomized control study conducted in rats selected to receive permissive hypercarbia after a transient global cerebral ischemic injury, mild-to-moderate hypercapnia ($PaCO_2$ of 60–100 mm Hg) was found to be neuroprotective after transient global cerebral ischemia-reperfusion injury (Zhou et al., 2010). Zhou and colleagues showed that mild-to-moderate hypercapnia (80–100 mm Hg) was associated with fewer histopathological changes and reduced cerebral apoptosis, which lead to better neurological deficit scores when compared with other levels of $PaCO_2$ (60–80 or 100–120 mm Hg). The authors theorize that mild-to-moderate hypercarbia interferes with apoptosis-regulating proteins, brain oxygen tension, and interaction with neurotransmitters, thus decreasing cell death and increasing neurological deficits scores (Zhou et al., 2010). The benefits of hypercapnia were not unlimited; in fact, severe hypercapnia ($PaCO_2$ of 100–120 mm Hg) increased brain injury (Zhou et al., 2010). Although examined in animal models, few studies have examined the effects of permissive hypercapnia in brain-injured patients.

In a small retrospective study conducted in 12 patients with both subarachnoid hemorrhage and ARDS, a lung protective strategy (i.e., tidal volume of 5–8 ml/kg and PEEP of 10–15 cm H_2O) was employed with resulting hypercapnia (pCO_2 of 50–60 mm Hg; Petridis et al., 2010). The researchers showed that, despite hypercapnia, there was no increase in intracerebral pressure. Findings from prior experimental studies in baboons with ischemic injuries indicated that the major cerebral arteries and the intracortical arteries of the brain constrict rather than dilate in the presence of hypercapnia, and the current authors use these data to support their findings (Mchedlishvili, Ormotsadze, Nikolaishvili, & Baramidze, 1967).

Although the results of these studies are thought provoking, caution needs to be used when applying these results in clinical practice. It is important to note in the Petridis et al. study that all the patients had subarachnoid hemorrhages with intracranial monitoring devices and a ventriculostomy that was draining

cerebral spinal fluid (Petridis et al., 2010). Also, the study was not randomized, and the sample size was small. As an editorial article written by Reinges highlights, ''the treatment reported in the paper by Petridis and colleagues…cannot generally be recommended until studies with a better design, especially controlled, randomized studies, have confirmed the results'' (Reinges, 2010). Specific questions to be addressed include as follows: Is the result reproducible in different and or larger patient subtypes (i.e., ischemic injuries), and what is the interaction of hypercapnia and ICP? Until better-designed randomized, controlled studies with larger populations conducted in humans are performed, the clinician cannot feel comfortable allowing their patients to experience uncontrolled hypercapnia based on the current data.

Conclusion

The management of ventilation in patients with both brain and lung injury remains challenging. Perhaps the best evidence gained from this review is support of preventive measures in intubated patients such as aspiration precautions, adequate mouth care, and daily sedation vacations when applicable. Because researchers continue to evaluate ventilation strategies to benefit patients, clinicians must cautiously evaluate the results of case reports and animal research studies. Although no treatment strategy can be recommended at this time to reconcile permissive hypercarbia for brain injury with permissive hypercarbia for lung injury, individualized treatment decisions may incorporate data reviewed here when conventional treatment is not providing safe, effective care. The goal of the clinician must be to balance the current neurological and pulmonary guidelines to meet the needs of the individual to provide the best possible outcome.

References

Afshari, A., Brok, J., Moller, A. M., & Wetterslev, J. (2011). Inhaled nitric oxide for acute respiratory distress syndrome and acute lung injury in adults and children: A systematic review with meta-analysis and trial sequential analysis. *Anesthesia and Analgesia, 112*(6), 1411–1421. doi:10.1213/ANE.0b013e31820bd185

Australia and New Zealand Extracorporeal Membrane Oxygenation Influenza Investigators, Davies, A., Jones, D., Bailey, M., Beca, J., Bellomo, R., … Ziegenfuss, M. (2009). Extracorporeal membrane oxygenation for 2009 influenza A(H1N1) acute respiratory distress syndrome. *Journal of the American Medical Association, 302*(17), 1888–1895. doi:10.1001/jama.2009.1535; 10.1001/jama.2009.1535

Bein, T., Scherer, M. N., Philipp, A., Weber, F., & Woertgen, C. (2005). Pumpless extracorporeal lung assist (pECLA) in patients with acute respiratory distress syndrome and severe brain injury. *Journal of Trauma, 58*(6), 1294–1297.

Bennett, S. S., Graffagnino, C., Borel, C. O., & James, M. L. (2007). Use of high frequency oscillatory ventilation (HFOV) in neurocritical care patients. *Neurocritical Care, 7*(3), 221–226. doi:10.1007/s12028-007-0084-y

Bentzer, P., Mattiasson, G., McIntosh, T. K., Wieloch, T., & Grande, P. O. (2001). Infusion of prostacyclin following experimental brain injury in the rat reduces cortical lesion volume. *Journal of Neurotrauma, 18*(3), 275–285. doi:10.1089/08977150151070919

Bernard, G. R., Artigas, A., Brigham, K. L., Carlet, J., Falke, K., Hudson, L., … Spragg, R. (1994). Report of the American–European consensus conference on acute respiratory distress syndrome: Definitions, mechanisms, relevant outcomes, and clinical trial coordination. consensus committee. *Journal of Critical Care, 9*(1), 72–81.

Brain Trauma Foundation, American Association of Neurological Surgeons, & Congress of Neurological Surgeons. (2007). Guidelines for the management of severe traumatic brain injury. *Journal of Neurotrauma, 24*(1), S1–S106.

Brower, R. G. (2002). Mechanical ventilation in acute lung injury and ARDS: Tidal volume reduction. *Critical Care Clinics, 18*(1), 1–13.

Chan, K. P., Stewart, T. E., & Mehta, S. (2007). High-frequency oscillatory ventilation for adult patients with ARDS. *Chest, 131*(6), 1907–1916. doi:10.1378/chest.06-1549

Contant, C. F., Valadka, A. B., Gopinath, S. P., Hannay, H. J., & Robertson, C. S. (2001). Adult respiratory distress syndrome: A complication of induced hypertension after severe head injury. *Journal of Neurosurgery, 95*(4), 560–568. doi:10.3171/jns.2001.95.4.0560

David, M., Karmrodt, J., Weiler, N., Scholz, A., Markstaller, K., & Eberle, B. (2005). High-frequency oscillatory ventilation in adults with traumatic brain injury and acute respiratory distress syndrome. *Acta Anaesthesiologica Scandinavica, 49*(2), 209–214. doi:10.1111/j.1399-6576.2004.00570.x

David, M., Markstaller, K., Depta, A. L., Karmrodt, J., Herweling, A., Kempski, O., … Gervais, H. W. (2006). Initiation of high-frequency oscillatory ventilation and its effects upon cerebral circulation in pigs: An experimental study. *British Journal of Anaesthesia, 97*(4), 525–532. doi:10.1093/bja/ael215

Dunham, C. M., Barraco, R. D., Clark, D. E., Daley, B. J., Davis, F. E, 3rd, Gibbs, M. A., … EAST Practice Management Guidelines Work Group. (2003). Guidelines for emergency tracheal intubation immediately after traumatic injury. *Journal of Trauma, 55*(1), 162–179. doi:10.1097/01.ta.0000083335.93868.2c

Eberhard, L. W., Morabito, D. J., Matthay, M. A., Mackersie, R. C., Campbell, A. R., Marks, J. D., … Pittet, J. F. (2000). Initial severity of metabolic acidosis predicts the development of acute lung injury in severely traumatized patients. *Critical Care Medicine, 28*(1), 125–131.

Faul, M., Xu, L., Wald, M. M., & Coronado, V. G. (2010). *Traumatic brain injury in the United States: Emergency department visits, hospitalizations and deaths 2002–2006*. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control.

Georgiadis, D., Schwarz, S., Baumgartner, R. W., Veltkamp, R., & Schwab, S. (2001). Influence of positive end-expiratory pressure on intracranial pressure and cerebral perfusion pressure in patients with acute stroke. *Stroke: A Journal of Cerebral Circulation, 32*(9), 2088–2092.

Grande, P. O., Moller, A. D., Nordstrom, C. H., & Ungerstedt, U. (2000). Low-dose prostacyclin in treatment of severe brain trauma evaluated with microdialysis and jugular bulb oxygen measurements. *Acta Anaesthesiologica Scandinavica, 44*(7), 886–894.

Gritti, P., Lanterna, L. A., Re, M., Martchenko, S., Olivotto, P., Brembilla, C., … Lorini, F. L. (2012). The use of inhaled nitric oxide and prone position in an ARDS patient with severe traumatic brain injury during spine stabilization. *Journal of Anesthesia, 27*, 293–297. doi:10.1007/s00540-012-1495-2

Hall, J. (2011). *Guyton and hall textbook of medical physiology* (12th ed.). Philadelphia, PA: Saunders.

Heuer, J. F., Sauter, P., Barwing, J., Herrmann, P., Crozier, T. A., Bleckmann, A., … Quintel, M. (2011). Effects of high-frequency oscillatory ventilation on systemic and cerebral hemodynamics and tissue oxygenation: An experimental study in pigs. *Neurocritical Care, 17*, 281–292. doi:10.1007/s12028-011-9566-z

Holland, M. C., Mackersie, R. C., Morabito, D., Campbell, A. R., Kivett, V. A., Patel, R., … Pittet, J. F. (2003). The development of acute lung injury is associated with worse neurologic outcome in patients with severe traumatic brain injury. *Journal of Trauma, 55*(1), 106–111. doi:10.1097/01.TA.0000071620.27375.BE

Lanken, P. N. (2005). Chapter 38: Acute lung injury and the acute respiratory distress syndrome. In J. B. Hall, G. A. Schmidt, & L. D. Wood (eds.), *Principles of critical care* (3rd ed., 5515–5548). New York, NY: McGraw Hill.

Leloup, G., Roze, H., Calderon, J., & Ouattara, A. (2011). Use of two oxygenators during extracorporeal membrane oxygenator for a patient with acute respiratory distress syndrome, high-pressure ventilation, hypercapnia, and traumatic brain injury. *British Journal of Anaesthesia, 107*(6), 1014–1015. doi:10.1093/bja/aer365

Levy, B., Bollaert, P. E., Nace, L., & Larcan, A. (1995). Intracranial hypertension and adult respiratory distress syndrome: Usefulness of tracheal gas insufflation. *Journal of Trauma, 39*(4), 799–801.

Lowson, S. M. (2002). Inhaled alternatives to nitric oxide. *Anesthesiology, 96*(6), 1504–1513.

Martinez-Perez, M., Bernabe, F., Pena, R., Fernandez, R., Nahum, A., & Blanch, L. (2004). Effects of expiratory tracheal gas insufflation in patients with severe head trauma and acute lung injury. *Intensive Care Medicine, 30*(11), 2021–2027. doi:10.1007/s00134-004-2439-6

Mascia, L. (2009). Acute lung injury in patients with severe brain injury: A double hit model. *Neurocritical Care, 11*(3), 417–426. doi:10.1007/s12028-009-9242-8

Mateen, F. J., Muralidharan, R., Shinohara, R. T., Parisi, J. E., Schears, G. J., & Wijdicks, E. F. (2011). Neurological injury in adults treated with extracorporeal membrane oxygenation. *Archives of Neurology, 68*(12), 1543–1549. doi:10.1001/archneurol.2011.209

McGuire, G., Crossley, D., Richards, J., & Wong, D. (1997). Effects of varying levels of positive end-expiratory pressure on intracranial pressure and cerebral perfusion pressure. *Critical Care Medicine, 25*(6), 1059–1062.

Mchedlishvili, G. I., Ormotsadze, L. G., Nikolaishvili, L. S., & Baramidze, D. G. (1967). Reaction of different parts of the cerebral vascular system in asphyxia. *Experimental Neurology, 18*(2), 239–252.

Muench, E., Bauhuf, C., Roth, H., Horn, P., Phillips, M., Marquetant, N., … Vajkoczy, P. (2005). Effects of positive end-expiratory pressure on regional cerebral blood flow, intracranial pressure, and brain tissue oxygenation. *Critical Care Medicine, 33*(10), 2367–2372.

Nemer, S., Santos, R., Caldeira, J., Reis, P., Guimarães, B., Loureiro, T., … Turon, R. (2011). Positive end-expiratory pressure can increase brain tissue oxygen pressure in hypoxemic severe traumatic brain injury patients. *Critical Care, 15*(Suppl 2), P41. doi:10.1186/cc10189

Papadimos, T. J., Medhkour, A., & Yermal, S. (2009). Successful use of inhaled nitric oxide to decrease intracranial pressure in a patient with severe traumatic brain injury complicated by acute respiratory distress syndrome: A role for an anti-inflammatory mechanism? *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine, 17*, 5. doi:10.1186/1757-7241-17-5

Peek, G. J., Mugford, M., Tiruvoipati, R., Wilson, A., Allen, E., Thalanany, M. M., … CESAR Trial Collaboration. (2009). Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): A multicentre randomised controlled trial. *Lancet, 374*(9698), 1351–1363. doi:10.1016/S0140-6736(09)61069-2; 10.1016/S0140-6736(09)61069-2

Petridis, A. K., Doukas, A., Kienke, S., Maslehaty, H., Mahvash, M., Barth, H., & Mehdorn, H. M. (2010). The effect of lung-protective permissive hypercapnia in intracerebral pressure in patients with subarachnoid haemorrhage and ARDS. A retrospective study. *Acta Neurochirurgica, 152*(12), 2143–2145. doi:10.1007/s00701-010-0761-z

Rangel-Castilla, L., Gopinath, S., & Robertson, C. S. (2008). Management of intracranial hypertension. *Neurologic Clinics, 26*(2), 521–541. doi:10.1016/j.ncl.2008.02.003

Ravenscraft, S. A., Burke, W. C., Nahum, A., Adams, A. B., Nakos, G., Marcy, T. W., & Marini, J. J. (1993). Tracheal gas insufflation augments CO2 clearance during mechanical ventilation. *American Review of Respiratory Disease, 148*(2), 345–351.

Reinges, M. H. (2010). Pros and cons of permissive hypercapnia in patients with subarachnoid haemorrhage and ARDS. *Acta Neurochirurgica, 152*(12), 2173–2174. doi:10.1007/s00701-010-0760-0

Rincon, F., Ghosh, S., Dey, S., Maltenfort, M., Vibbert, M., Urtecho, J., … Jallo, J. (2012). Impact of acute lung injury and acute respiratory distress syndrome after traumatic brain injury in the United States. *Neurosurgery, 71*, 795–803. doi:10.1227/NEU.0b013e3182672ae5

Rodriguez, E. (2013). *Extracorporeal membrane oxygenation*. Retrieved from http://emedicine.medscape.com/article/1818617-overview#aw2aab6b5

Stiefel, M. F., Zaghloul, K. A., Bloom, S., Gracias, V. H., & LeRoux, P. D. (2007). Improved cerebral oxygenation after high-dose inhaled aerosolized prostacyclin therapy for acute lung injury: A case report. *Journal of Trauma, 63*(5), 1155–1158. doi:10.1097/TA.0b013e31815965e3

Theodore, J., & Robin, E. (1975). Pathogenesis of neurogenic pulmonary œdema. *Lancet, 306*(7938), 749–751. doi:10.1016/S0140-6736(75)90729-1

Vanhoonacker, M., Roeseler, J., & Hantson, P. (2012). Reciprocal influence of refractory hypoxemia and high intracranial pressure on the postoperative management of an urgent neurosurgical procedure. *Respiratory Care, 57*(7), 1186–1190. doi:10.4187/respcare.01322; 10.4187/respcare.01322

Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. (2000). *New England Journal of Medicine, 342*(18), 1301–1308. doi:10.1056/NEJM200005043421801

Wunsch, H., & Mapstone, J. (2004). High-frequency ventilation versus conventional ventilation for treatment of acute lung injury and acute respiratory distress syndrome. *Cochrane Database of Systematic Reviews (Online),* (1), CD004085. doi:10.1002/14651858.CD004085.pub2

Wunsch, H., Mapstone, J., & Takala, J. (2005). High-frequency ventilation versus conventional ventilation for the treatment of acute lung injury and acute respiratory distress syndrome: A systematic review and cochrane analysis. *Anesthesia and Analgesia, 100*(6), 1765–1772. doi:10.1213/01.ANE.0000145070.52315.F2

Young, N. H., & Andrews, P. J. (2011). High-frequency oscillation as a rescue strategy for brain-injured adult patients with acute lung injury and acute respiratory distress syndrome. *Neurocritical Care, 15*(3), 623–633. doi:10.1007/s12028-011-9550-7

Zhou, Q., Cao, B., Niu, L., Cui, X., Yu, H., Liu, J., … Li, W. (2010). Effects of permissive hypercapnia on transient global cerebral ischemia-reperfusion injury in rats. *Anesthesiology, 112*(2), 288–297. doi:10.1097/ALN.0b013e3181ca8257

Instructions for Taking the CE Test:

- Read the article. The test for this CE activity can be taken online at www.NursingCenter.com/CE/JNN.
- There is only one correct answer for each question. A passing score for this test is 13 correct answers. If you pass, you can print your certificate of earned contact hours and the answer key. If you fail, you have the option of taking the test again at no additional cost.
- If you prefer to mail in the test, access it and the enrollment form at www.JNNOnline/CE. Print the enrollment form and mail it with payment to the address listed. You will receive your earned CE certificate in 4 to 6 weeks.
- Visit www.nursingcenter.com for other CE activities and your personalized CE planner tool.
- For questions or rush service options, contact Lippincott Williams & Wilkins: 1-800-787-8985.

Registration Deadline: April 30, 2016

Disclosure Statement:

The author and planners have disclosed that they have no financial relationships related to this article.

Provider Accreditation:

Lippincott Williams & Wilkins, publisher of *Journal of Neuroscience Nursing*, will award 2.5 contact hours for this continuing nursing education activity.

Lippincott Williams & Wilkins is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

This activity is also provider approved by the California Board of Registered Nursing, Provider Number CEP 11749 for 2.5 contact hours. Lippincott Williams & Wilkins is also an approved provider of continuing nursing education by the District of Columbia and Florida CE Broker #50-1223. Your certificate is valid in all states.

The ANCC's accreditation status of Lippincott Williams & Wilkins Department of Continuing Education refers only to its continuing nursing educational activities and does not imply Commission on Accreditation approval or endorsement of any commercial product.

Payment and Discounts:

- The registration fee for this test is $24.95.
- AANN members – For free CE (online only), members can take the test by logging into the secure "Members Only" area of http://www.aann.org to get the discount code. Use the code when payment is requested when taking the CE test at NursingCenter.com/CE/JNN.
- We offer special discounts and institutional bulk discounts for multiple tests. Call 1-800-787-8985 for more information.