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Chapter

Mechanical Ventilation in Neurocritical Patients

Thierry Hernández-Gilsoul, Jose de Jesús Vidal-Mayo and Alan Alexis Chacon-Corral

Abstract

Patients under neurocritical care may require mechanical ventilation for airway protection; respiratory failure can occur simultaneously or be acquired during the ICU stay. In this chapter, we will address the ventilatory strategies, in particular the role of protective lung ventilation, and the potential increase in intracranial pressure as a result of permissive hypercapnia, high airway pressures during recruitment maneuvers, and/or prone position. We will also describe some strategies to achieve mechanical ventilation liberation, including evaluation for tracheostomy, timing of tracheostomy, mechanical ventilation modalities for weaning and extubation, or tracheostomy weaning for mechanical ventilation.

Keywords: mechanical ventilation, neurocritical

1. Introduction

Neurological critically ill patients represent an important group in the intensive care unit (ICU) worldwide. About 20% of these patients require mechanical ventilation (MV) of which 20–25% will develop acute respiratory distress syndrome (ARDS) [1, 2]. Ventilatory management is controversial in this kind of population due to the complexity of the event and singularity of each case with acute brain injury (ABI). This includes traumatic brain injury (TBI), intracerebral hemorrhage (ICH), aneurysmatic subarachnoid hemorrhage (aSH), acute ischemic stroke (AIS), and other entities associated with high intracranial pressure (ICP). Additionally, brain damage may be prevented by avoiding pulmonary and systemic injury associated with mechanical ventilation. Thus, this topic is particularly important, since respiratory failure is the most frequent extracerebral organic failure in patients with ABI [3].

Recently, the VENTILA group reported some interesting characteristics, in the evolution of the ventilatory management in neurological critically ill patients, in three cohorts of patients with mechanical ventilation (2004, 2010, and 2016) [4]. In this multicentric international report of 4152 patients, the main pathologies were intracerebral hemorrhage and traumatic brain injury. One of the main results was an increment in the use of lung protective ventilation through time (47% in 2004, 63% in 2010 vs 65% in 2016; $p<0.001$). However, there were no differences in other outcomes such as length of stay in ICU, length of stay in hospital, mortality in the ICU, and mortality in the hospital. Some variables were associated with mortality in multivariate analyses such as age > 75 years old (OR 1.80, CI 95% 1.40–2.30),

SAPS II (Simplified Acute Physiology Score II) > 50 points (OR 2.31, CI 95% 1.87–2.86), occurrence of organic failure within the first 48 h after ABI (OR 1.79, IC 95% 1.59–2.0), and etiology of ABI, specifically TBI (OR 1.8, CI 95% 1.4–2.3), ischemic stroke (OR 3.94, CI 95% 2.47–6.31), and cerebral hemorrhage (OR 3.96, CI 95% 2.59–6.06).

2. Brain-lung cross talking

Acute brain injury can create issues in lung function and vice versa. This bidirectional brain-lung interaction is supported in experimental models and basic studies in humans, which have shown several neuroinflammatory, autonomic, immunologic, and endocrine pathways [5]. According to the so-called two-stroke model, when ACL occurs, a lung injury associated with systemic inflammation due to a "catecholamine storm" appears, first hit; subsequently these events can trigger an increase in permeability into the pulomnary capillaries, vasoconstriction in the pulmonary arterioles and recruitment of inflammatory cells in the alveoli, second hit [6].

Hypoxemia and hypercapnia are associated with lung injury and amplify acute brain injury. Both situations reduce cerebral vascular resistance, which consequently raises cerebral blood flow and increases ICP. Also, they can increase the systemic inflammatory response and produce extracerebral organic failures. In the literature, this chain of events had been denominated *dangerous cross talk* [7, 8]. Thus, ventilatory management has been considered a strategy to avoid ventilator-induced lung injury (VILI) through the use of lung-protective ventilation.

3. Ventilatory management

The most recent guidelines related to this topic are provided by the European Society of Intensive Care Medicine [9]. Evidence about most of these recommendations remains at a low level; for this reason, we present the most general suggestions in order to give a safety and efficient ventilatory management to these patients.

3.1 Oxygenation and carbon dioxide (CO_2) targets

In patients with ABI, it is fundamental to guarantee an optimal oxygenation to avoid secondary brain injury [10]. It is recommended to target "normoxia" with a partial arterial pressure of oxygen (PaO_2) between 80-120 mmHg and or a peripheral oxygen saturation (SpO_2) of ≥95% in patients with or without intracranial hypertension [9, 11].

In addition, some evidence suggests that hyperoxia is an independent factor associated to greater mortality and outcomes driven by several mechanisms: vasoconstriction of brain arteries, synthesis of reactive oxygen species (ROS) and damage associated molecular patterns (DAMPs) [10]. In a clinical trial of patients with traumatic brain injury (TBI), which evaluated two oxygenation strategies (normobaric hyperoxia and normoxia), there were no differences in the hospital length of stay, but the modified Rankin scale at discharge and at 6 month follow-up was better in the normoxia group [12].

In relation to the minute ventilation settings (respiratory rate times tidal volume) to modify the CO_2 content of the blood, it is recommended to adjust the ventilation to maintain normal levels of arterial pressure of carbon dioxide ($PaCO_2$) between 35 and 45 mmHg. Traditionally, it was considered that patients with ABI (specially population with TBI) should be maintained with hyperventilation;

however, this situation can lead to cerebral vasoconstriction that can worsen cerebral tissue hypoxia and ischemia [13]. In a randomized clinical trial conducted by Muizelaar et al., it found that patients with TBI undergoing systematic hyperventilation ($PaCO_2$ 25 ± 2 mmHg) had poorer outcomes at 3 and 6 months' follow-up compared with the normocapnia group ($PaCO_2$ 35 ± 2 mmHg). Deleterious findings were also documented in head injury patients who were managed with hyperventilation plus tromethamine addition as buffer [14]. Transient hyperventilation ($PaCO_2$ 30–35 mmHg) is only recommended as a rescue maneuver in cases of brain herniation [9].

3.2 Tidal volume (Vt)

Ventilation with Vt between 6 and 8 ml/kg of predicted body weight is considered a standard of ventilatory treatment in patients with ARDS and its application in general in patients under invasive ventilatory support. However, historically, neurocritical patients have been excluded from clinical trials that have evaluated this ventilatory therapeutic strategy due to the potential increase in intracranial pressure caused by hypercapnia and increased intrathoracic pressures [15].

In a multicenter cohort study, it was found that an average Vt of 9 ml/kg of predicted weight was used in this group of patients [15]. Additionally, it has been described that the use of high Vt has been associated with the development of ARDS in these patients [16] while other observational studies have found no evidence of this association; instead, driving pressure was the only ventilatory variable associated with the development of ARDS [17]. Likewise, there is no consistent evidence that the use of a Vt by itself increases intracranial pressure [15, 18].

A recent multicenter prospective study that used a strategy of low Vt (less than 7 ml/kg), moderate PEEP (6–8 cmH_2O), and a protocol for early extubation was associated with more days free of mechanical ventilation and lower mortality at 90 days, with no serious adverse events associated with this intervention [19]. Condensing this information, the administration of Vt of 6–8 ml/kg is suggested to maintain a plateau pressure of less than 25 cmH_2O and a driving pressure of less than 15 cmH_2O [8, 11, 13].

3.3 Positive end expiratory pressure (PEEP)

Implementation of PEEP associated with low Vt in the pulmonary protective ventilation strategy has been associated with better clinical outcomes, even in patients without ARDS [20]. Its use has been a useful strategy in neurocritical patients where oxygenation and ventilation are essential. The PEEP level has been considered a potential indirect maneuver that increases ICP in a directly proportional way. This led Asehnoune et al. to study the use of PEEP and its effect on intracranial pressure, comparing PEEP levels less than or greater than 5 cmH_2O; no clinically significant differences of episodes of intracranial hypertension were seen [19]. Boone et al. analyzed 341 patients with ABI, in which nonsignificant effects of PEEP on ICP or cerebral perfusion pressure (CPP) were documented [21]. Furthermore, in a study of patients with aSH divided into groups according to respiratory compliance, those with decreased respiratory compliance (<45 ml/cmH_2O) did not show changes in the hemodynamic variables, including CPP at diverse levels of PEEP [22].

In another prospective study of 20 patients with TBI with brain-tissue oxygenation ($P_{bt}O_2$) monitorization, an increase in the level of PEEP from 5 to 10 cmH_2O (24.60 ± 6.84 to 26.55 ± 7.09; $p = 0.0001$) and from 10 to 15 cmH_2O (26.55 ± 7.09 to 29.05 ± 7.07; $p = 0.0001$) significantly increased $P_{bt}O_2$ in these patients, without significant changes in ICP or CPP [23].

Therefore, it is recommended to administer a sufficient PEEP (5–8 cmH_2O) to maintain adequate oxygenation. In cases where PEEP is greater than 10–15 cmH_2O, it is suggested that advanced neuromonitoring be used to adjust this variable optimally [11, 13, 24].

3.4 Prone positioning

Mechanical ventilation in the prone position is also a standard of treatment for patients with moderate-severe ARDS, since it reduces mortality in addition to improving oxygenation, respiratory mechanics, and ventilation-perfusion imbalance. However, due to the potential increase in ICP and reduction in CCP, these patients have also been excluded from clinical studies to evaluate this intervention [13].

In an observational study of patients with aSH, who fulfilled criteria for ARDS within the first 2 weeks, a significant increase in oxygenation was found (97.3 ± 20.7 mmHg in the supine position to 126.6 ± 31.7 mmHg in the prone position) as well as an increase in $P_{bt}O_2$ (26.8 ± 10.9 mmHg to 31.6 ± 12.2 mmHg; $p < 0.0001$) with a good tolerance of the intervention (prone position for 14 hours). In contrast to a concomitant increase in ICP and a decrease in CPP, however, overall, the benefit in systemic oxygenation was greater than the effects on cerebral perfusion and intracranial pressure [25].

In the same way, other observational studies have reported that this maneuver improves patient oxygenation and $P_{bt}O_2$ with a tendency to increase ICP but without reducing CPP. One report with 8 patients showed a significant increase in oxygenation with an increase in ICP and CPP as well as an improvement in $P_{bt}O_2$ [26]. Roth et al. found in a retrospective study that patients had a significant increase in oxygenation with an increase in ICP without significant changes in CPP [27].

Recommendations in this group of patients suggest ventilation in the prone position. In patients with moderate-severe ARDS without evidence of intracranial hypertension, it is a safe and effective strategy. However, the risks and benefits of the intervention should be considered, and the patient must have multimodal monitoring to determine the effects on both systemic and cerebral hemodynamics and oxygenation [9, 11].

3.5 Alveolar recruitment maneuvers

Another controversial aspect is the use of alveolar recruitment maneuvers, due to the potential risk of increasing intracranial pressure with reduction of CPP [13]. In systematic reviews and meta-analysis of ARDS studies, it was found that this intervention is associated with an improvement in the oxygenation of patients but without effects in other outcomes such as mortality or duration of mechanical ventilation [28, 29].

In studies carried out in this population, conflicting results have been found regarding the efficacy of this intervention to improve oxygenation; however, regarding neurological variables, some studies described an increase in ICP associated with a decrease in CPP without improvement in oxygenation [30, 31]; another study found that recruitment maneuvers significantly affected cerebral hemodynamics [32].

Although the most recent guidelines for ventilatory management of these patients do not issue any recommendation due to limited evidence [9], expert recommendations suggest that this intervention can be considered individually in patients with acute brain injury and concomitant ARDS with an invasive neuromonitoring for the potential risks and benefits of these maneuvers [8, 13].

4. Extracorporeal life support (ECLS)

Extracorporeal membrane oxygenation ventilation (ECMO) and extracorporeal CO_2 removal ($ECCO_2R$) have gained popularity for patients with hypoxemic respiratory failure refractory to conventional ventilation strategies; however, because the evidence for this intervention is anecdotal in this patient population [33, 34] and there is a risk of catastrophic complications in patients with ABI (especially intracranial hemorrhage due to the need for routine anticoagulation), there is no consensus to carry out this intervention in neurocritical patients [9, 11, 13]. Heparin-free regional citrate anticoagulation, like in renal replacement circuits, may offer an alternative to this problem [35]. The use of regional citrate anticoagulation continuous veno-venous hemofiltration (RCA-CVVH) connected to an ECMO circuit, with low heparin or heparin-free ECMO, has been reported [36].

In an experimental model of severe hypercapnic acidosis, regional anticoagulation with citrate solution achieved the anticoagulation goal as well as standard heparin anticoagulation but did not improve CO_2 removal and led to more hypocalcemia and hypotension [37].

5. Weaning from mechanical ventilation

Historically, the population of neurocritical patients has been considered at high risk of failure to extubation (from 10 to 38% failure), and hence there is delayed withdrawal of mechanical ventilation which is associated with higher rates of ventilator associated pneumonia (VAP) and airway injury; longer mechanical ventilation and ICU length stay, and higher mortality [15, 38, 39].

The recommendations of the international guidelines for the withdrawal of mechanical ventilation do not contemplate specific aspects for this population [40, 41], in addition to the fact that certain general aspects of these consensuses are not applicable for neurocritical patients:

- The process by which the patient is on mechanical ventilation is not resolved in most cases of patients with ABI [3, 39, 42].

- Evaluation of the state of consciousness (and, therefore, the ability to follow commands) is altered in a significant proportion of patients. In addition, scales used for the neurological evaluation in neurocritical patients on mechanical ventilation do not precisely discriminate success versus failure after extubation [40, 41]. Some studies have found that a score greater than 8 or greater than 10 in Glasgow Coma Scale (GCS) is associated with a successful withdrawal from mechanical ventilation [43, 44], while other series found that neither the GCS [42] nor the FOUR scale [45] was associated with successful extubation.

There is evidence that multidisciplinary and standardized protocols in these patients are associated with better outcomes and a higher rate of successful withdrawal from mechanical ventilation [46, 47]. One tool designed for this population is the VISAGE score by Asehnoune et al [44]. This score was derived from a multicenter prospective cohort that included a heterogeneous population of patients with ABI (n = 437), of which 77.3% had a successful extubation. From the multivariate analysis of the factors associated with successful extubation, 4 variables with significant association were found that made up the VISAGE score: visual pursuit, swallowing attempts, age under 40 years, and GCS greater than 10 points (**Table 1**). According to the original validation study, a score on this scale greater than or equal to 3 points

A score ≥ 3 is associated with 90% extubation success; each variable has a value of 1 point • Age < 40 years • Visual pursuit • Swallowing attempts • Glasgow coma score > 10 points
[44].

Table 1.
VISAGE score.

has a sensitivity of 62%, specificity of 79%, positive predictive value of 90%, negative predictive value of 39%, positive likelihood ratio of 2.9, and negative likelihood ratio of 0.5 to predict extubation success. This scale represents a practical tool for use in the patient's bed, for which several experts have recommended its clinical use; however, external validation in other patient cohorts is still pending [48, 49].

In a systematic review with meta-analysis, Wang et al. found that other variables associated with extubation failure in neurocritical patients are the presence of pneumonia, atelectasis, mechanical ventilation for more than 24 h, a score of GCS lower than 8 (OR = 4.96.95% CI = 1.61–15.26, p = 0.005), the inability to follow orders (OR = 2.07.95% CI = 1.15–3.71, p = 0.02), thick secretions, and alteration in cough reflex [50]. Another score that evaluates the ability to protect the airway has been proposed (the Airway score), which takes into consideration variables such as the amount and quality of respiratory secretions, gag and cough reflex, and patients with a score of less than 6 who are candidates for IMV withdrawal. Nevertheless, it should be considered that there is a wide variability in the qualitative assessment of respiratory secretions and that there is no extensive external validation of this tool [51].

Regarding the actual evidence of tracheostomy performance, it has been observed that intensivist achieves more frequently tracheostomies in neurocritical patients (up to 45%) compared to general patients in the ICU [52]. The theorical benefits of tracheostomy are that it decreases the work of breathing and improves patient comfort when compared to an endotracheal tube. Tracheal stoma that does not generate pain after 48–72 h of tracheostomy placement. Reduction or suspension of sedation and opioid analgesia, as well as less work of breathing are the theorical benefits that generate greater patient comfort. Contrary to general belief, there is no evidence that it decreases the frequency of tracheal stenosis associated with prolonged ventilation. Even more, an endotracheal cannula also requires the inflation of a balloon to isolate and protect the airway from bronchoaspiration; thus, tracheal stenosis is also a complication, which according to a case study is more complicated (infraglottic stenosis) and may not resolve more frequently compared to tracheal stenosis acquired with an orotracheal tube [53].

According to this information and consensus, it is recommended to consider to facilitate the withdrawal of mechanical ventilation in the following cases: infratentorial lesions, inability to protect the airway (inadequate management of respiratory secretions), altered central respiratory drive, slow or unfavorable neurological recovery, and patients with recurrent extubation failure.

However, the precise indications for its performance and the timing of the intervention remain poorly defined in the literature [38, 48, 54].

A highly controversial aspect is the performance of "early tracheostomy," which has been defined as placing it within the first 7 days [55] (there are reports that define it from day 5 to day 10) of mechanical ventilation [56, 57].

Large series of patients that have compared early versus late tracheostomy have not found a benefit in terms of mortality, although there is a trend of better

outcomes in the early tracheostomy group, such as reduction in the frequency of ventilator-associated pneumonia, fewer days of mechanical ventilation, and a shorter length of stay in intensive care [58, 59]. In the SETPOINT study (Stroke-related Early Tracheostomy vs. Prolonged Orotracheal Intubation in Neurocritical care Trial) that randomized 60 patients with stroke or cerebral hemorrhage to early tracheostomy (day 1–3 of mechanical ventilation) versus standard tracheostomy (between 7 and 14 days), no difference was found in the primary endpoint, which was the length of stay in the ICU (median, interquartile range [IQR] 8, 16–28 days versus 17 [13–22] days, median difference: 1 [−2 to 6]; $p = 0.38$) although in the intervention group, mortality in the ICU and at 6 months was significantly lower (10 versus 14%; $p < 0.01$ and 27% versus 60% $p = 0.02$), without finding other differences in other secondary outcomes [60].

The CENTER-TBI study that was a prospective European multicenter cohort of adult patients with head trauma found that the factors associated with the decision to perform a tracheostomy were older age (HR = 1.04, 95% CI 1.01–1.07; $p = 0.003$), GCS less than or equal to 8 (HR = 1.70, 95% CI = 1.22–2.36 at 7; $p < 0.001$), thoracic trauma (HR = 1.24, 95% CI = 1.01–1.52, $p = 0.020$), hypoxemia (HR = 1.37, 95% CI = 1.05–1.79, $p = 0.048$), and absence of pupillary reactivity (HR = 1.76, 95% CI = 1.27–2.45 at 7; $p < 0.001$). Additionally, a wide heterogeneity was identified in the frequency (7.9–50.2%) and timing of early tracheostomy practice (0–17.6%) in

	Points
Neurological function	
Dysphagia (4 points)	4
Observed aspiration (3 points)	3
GCS on admission < 10 (3 points)	3
Neurological lesion	
Brain stem (4 points)	4
Ischemic stroke > 2/3 middle cerebral artery territory (4 points)	4
ICH volume > 25 ml (4 points)	4
Hydrocephalus (4 points)	4
Space-occupying cerebellar (3 points)	3
Diffuse lesion (3 points)	3
Extracerebral organ function-procedure	
APACHE II score > 20 (4 points)	4
Sepsis (3 points)	3
Additional respiratory disease (3 points)	3
PaO_2/FiO_2 < 150 (2 points)	2
LIS score > 1 (2 points)	2
Neurosurgical intervention (2 points)	2

A score > 8 in combination with an estimate of an experienced neurointensivist suggests prolonged ventilation and need of tracheostomy.
GCS = glasgow coma scale. ICH = intracerebral hemorrhage. PaO_2 = partial arterial pressure of oxygen. APACHE II = acute physiology and chronic health evaluation II. LIS = lung injury score.
[62, 63].

Table 2.
SET score to estimate tracheostomy need after severe stroke.

this cohort. Late tracheostomy (after 7 days) was associated with worse neurological outcomes and a longer stay in the intensive care unit [61].

In acute cerebrovascular events (ischemic stroke, cerebral hemorrhage, and aSH), a specific score for predicting tracheostomy has been designed and tested in these patients. The SET score (**Table 2**) that combines various variables from 3 items (neurological evaluation, characteristics of the injury, and extracerebral organic procedure/function) is the one with the greatest external validation for use in this population. A SET score of >10 points has a sensitivity of 64–81%, a specificity of 57–86%, and an area under the curve of 0.74 (95% CI 0.68–0.81) [62, 63].

In terms of an invasive procedure without complications, percutaneous tracheostomy is practically equivalent to surgical tracheostomy. Some systematic reviews with meta-analyses have found that the former has fewer stoma infections, with similar rates of bleeding and other procedural complications [64–66].

6. Conclusion

Neurocritical patients represent a particularly challenging subgroup for ventilatory management due to coexistence of acute brain injury associated with other organ failure, the most frequent being respiratory failure. Management of mechanical ventilation should prevent secondary brain injury by ensuring optimal ventilation and oxygenation. The use of additional strategies to standard management of pulmonary protective ventilation (high PEEP, recruitment maneuvers, and extracorporeal circulatory support) in patients with refractory respiratory failure should be individualized and be accompanied by advanced neuromonitoring (invasive measurement of intracranial pressure and cerebral tissue pressure oxygen). It is important to avoid a late withdrawal of mechanical ventilation using adjuvant scales such as the VISAGE score; theorical benefits from tracheostomy include reduction and suspension of sedation and opioid analgesia as well as patient comfort due to lower work of breathing and may be considered in patients with slow neurological recovery, failure to extubation, and those patients with dysphagia or altered state of consciousness resulting from a primary injury to the central nervous system.

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