Journal of Critical Care 50 (2019) 118–121

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.journals.elsevier.com/journal-of-critical-care

Airway pressure release ventilation does not increase intracranial pressure in patients with traumatic brain injury with poor lung compliance☆

Colston A. Edgerton [a], Stuart M. Leon [a], Melissa A. Hite [a], Stephen P. Kalhorn [b], Lancer A. Scott [c], Evert A. Eriksson [a,*]

[a] Department of Surgery, Division of Trauma and Critical Care, 96 Jonathan Lucas St. CSB 416, Medical University of South Carolina, Charleston, SC 29425, USA
[b] Department of Neurosurgery, 96 Jonathan Lucas St. Room 301 CSB, Medical University of South Carolina, Charleston, SC 29425, USA
[c] Department of Emergency Medicine, 169 Ashley Ave. Room 265 NT, Medical University of South Carolina, Charleston, SC 29425, USA

ARTICLE INFO

Keywords:
Traumatic Brain injury
Airway pressure release ventilation
Intracranial pressure
Airway compliance

ABSTRACT

The use of Airway Pressure Release Ventilation (APRV) in patients with traumatic brain injury (TBI) remains controversial. Some believe that elevated mean airway pressures transmitted to the thorax may cause clinically significant increases in Central Venous Pressure (CVP) and intracranial pressure (ICP) from venous congestion. We perform a retrospective review from 2009 to 2015 of traumatically injured patients who were transitioned from traditional ventilator modes to APRV and also had an ICP monitor in place. Fifteen patients undergoing 19 transitions to APRV were identified. Prior to transitioning to APRV the average static and dynamic compliance was 22.9 +/− 5.6 and 16.5 +/− 4.12 mL/cm H2O. There was no statistical difference in ICP, MAP, and CPP prior to and after transition to APRV. There was a statistically significant increase in CVP, PaO2, and P:F ratio. Individually, only 4 patients had ICP values >20 in the first hour after transitioning to APRV and the rate of ICP elevations was similar between the two modes of ventilation. These data show that APRV is a viable mode of ventilation in patients with TBI who have low lung compliance. The increased CVP of this mode of ventilation did not affect ICP or hemodynamic parameters.

1. Introduction

Patients with severe Traumatic Brain Injury (TBI) often require mechanical ventilation due to their neurologic injury alone, or because of multi-system trauma. Prolonged mechanical ventilation may result in decreased pulmonary compliance and alveolar collapse, leading to acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), which is associated with significant morbidity and higher mortality rates. APRV or "BiVent" is an advanced mode of mechanical ventilation that provides pressure controlled intermittent mandatory ventilation. It was first introduced into the literature in 1986, but its role as a standard versus rescue mode of ventilation in ARDS continues to be debated [1]. It allows for spontaneous breathing in addition to mandatory time triggered release to interrupt periods of elevated CPAP for ventilation. The I:E ratio is often around 4:1 which is notably higher than the 1:2–3 ratios seen in most modes of conventional lung protective ventilation. This higher I:E ratio is also a notable difference from Biphasic Positive Airway Pressure (BIPAP), and can lead to high mean airway pressures [2].

When transitioning a patient from more conventional methods of ventilation to APRV, the end-inspiratory pressure or plateau pressure is measured to serve as a reflection of alveolar volume and lung compliance. The High Airway Pressure, or "P_{high}" should equal this plateau pressure to avoid barotrauma. The pressure experienced during the release phase rarely reaches zero as a result of residual positive pressures associated with anatomical factors such as chest recoil and airway elastance that are still exerting an effect during this short interval. A second setting is the time at $P_{high,}$ which is often designated "T_{high}". This is usually adjusted such that the T_{high} is 85–90% of the total cycle time, including the time allowed for pressure release [3]. The advantages of APRV are improved arterial oxygenation that results from increased recruitment of the collapsed alveoli seen in ARDS and severe lung injury. This effect is often seen within 24 h. As a result of opening previously

☆ This manuscript has not been previously published in whole or in part or submitted elsewhere for review. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors have no disclosures or conflicts of interests to report.

* Corresponding author at: Department of Surgery, 96 Jonathan Lucas Street, CSB 416, Charleston, SC 29425, USA.
E-mail addresses: edgertoc@musc.edu (C.A. Edgerton), leon@musc.edu (S.M. Leon), hitema@musc.edu (M.A. Hite), kalhorn@musc.edu (S.P. Kalhorn), scottlan@musc.edu (L.A. Scott), evsurgery@gmail.com (E.A. Eriksson).

https://doi.org/10.1016/j.jcrc.2018.11.034
0883-9441/

de-recruited lung parenchyma, airway compliance is increased. An additional effect is that lower peak airway pressures are often seen while using this mode of ventilation [4].

An important physiologic consideration is that providing almost constant positive pressure to the thorax, the decrease in venous return seen in all modes of positive pressure ventilation is more pronounced. This can lead to reduced preload and decreased cardiac output in preload dependent states. It also leads to venous congestion, which becomes particularly important in patients with traumatic brain injuries. Cerebral Perfusion Pressure (CPP) is measured as the difference of the mean arterial pressure (MAP) and intracranial pressure (ICP), with the former often being more tenuous and volatile in multi-trauma patients, while normal physiologic methods to regulate the latter are altered. This results in relying on exogenous methods to control ICP and resulting CPP. Transitioning patients to a mechanical mode of ventilation that increases ICP secondary to decreased venous return can complicate this delicate balance further. The degree to which higher mean airway pressures are transmitted to the mediastinum and then to the cerebral venous system is thought to be dependent on airway compliance which is defined as the change in volume for a given change in pressure.

There is a paucity of data regarding the safety of APRV in TBI patients. A case report by Marik et al. highlights a patient with severe progressive hypoxemia following a subarachnoid hemorrhage who was converted from conventional pressure-controlled mechanical ventilation to APRV. The change saw better oxygenation and alveolar ventilation with an increase in cerebral blood flow and negligible increase in ICP [5]. This study supports the idea that APRV may safely be applied to patients with intracranial bleeds, and that it may increase cerebral blood flow without increasing ICP. High Frequency Percussive Ventilation (HFPV) is another high pressure mode of ventilation that has been shown by Salim and colleagues in a study of 10 patients to have significant improvement in oxygenation with concomitant reduction in ICP during the first 16 h of therapy [6]. One of the largest studies of APRV in TBI patients analyzes the 6 h following transition to APRV in 21 TBI patients with a primary outcome being therapeutic intensity level, which is a measure of the degree to which interventions are used to manage ICP. They demonstrated an increased but not clinically significant change in the therapeutic intensity level, decrease in ICPs, and no significant chance in CPP following transition to APRV [7]. Our study examines the physiologic effects of a transition to APRV on traumatically injured patients in whom ICP is continuously monitored.

2. Materials and methods

This retrospective review was conducted with approval of the Institutional Review Board. Patients were identified who were admitted to the Intensive Care Unit (ICU) from January 2009 – December 2015, with traumatic brain injury and intracranial monitor placement who were also transitioned from traditional ventilator modes to APRV. Patients were excluded if they were younger than 18 years old, underwent decompressive craniotomy, or had a non-traumatic neurologic insult. The trauma registry was used to determine injury characteristics as well as obtain laboratory data and hemodynamic parameters surrounding the transition in ventilation modes. Vital signs as well as ventilator settings and measurements were recorded for three hours before and after the transition to APRV. Pharmacologic dosing was also analyzed surrounding the transition to determine if medical management of ICP was done contemporaneously with the transition. Additionally, the number of ICP spikes above 20 were counted and divided by the number of hours on a particular mode of ventilation to determine an ICP spike rate for each mode of ventilation.

Normally distributed continuous variables are presented as mean +/− SD. Non-normally distributed continuous variables are presented as median and interquartile range. Continuous variables were compared between groups using the 2-tailed *t*-test. Categorical variables were compared between groups using the $\chi 2$-analysis. A p value<0.05 was used as a measure of statistical significance. SPSS version 24.0 (Chicago, IL) was used for all statistical analyses.

3. Results

Fifteen patients undergoing 19 transitions to APRV were identified. The average age of the cohort was 40 +/− 17 years old, 87% were male and the average ISS was 33.4 +/− 13.4. The average AIS head was 4.1 +/− 0.9 (Table 1). Prior to transitioning to APRV the average static and dynamic compliance was 22.9 +/− 5.6 and 16.5 +/− 4.12 mL/cm H2O (Table 2). Physiologic parameters are presented in Table 3 and were largely unchanged after the transition to APRV (ICP 12.7 +/− 4.3 vs. 13.5 +/− 3.4, $p = 0.356$; MAP 87.2 +/− 12.8 vs. 86.79 +/− 14.5, $p = 0.884$; CPP 74.5 +/− 11.6 vs. 73.3 +/− 14.0, $p = 0.672$). There was a significant change in CVP (9.7 +/− 4.8 vs. 14.2 +/− 5.9, $p = 0.041$). There was also an expected increase in P:F ratio (162±92 vs. 221+/− 116, $p = 0.035$) and PaO2 (100.3 +/− 38.1 vs. 138.2 +/− 49.0, $P \leq 0.001$). The patients' pH and arterial CO2 values were also not significantly different. Individually, only 4 patients had ICP values >20 in the first hour after transitioning to APRV and the rate of ICP elevations (# of ICP readings >20/h on mode of ventilation) was similar between the two modes of ventilation [0.067 #ICP > 20/h (0.018–0.217) vs. 0.025 #ICP > 20/h (0.000–0.128), $p = 0.332$] (Fig. 1). None of the patients received osmotic therapy or sedation/pain medication boluses to address intracranial pressure during the 6-h observation period surrounding the transition to APRV. None of the patients had a change in their basal sedation/pain management in the transition to APRV.

4. Discussion

This retrospective study examines the safety of APRV in patients with TBI. Several of the physiologic measurements seen following transition are to be expected and others warrant further examination. The overall goal of APRV is to improve oxygenation, and our data demonstrate this benefit is preserved in TBI patients failing conventional modes of ventilation. Improvement in both PaO2 and the P:F ration reached statistical significance following transition to APRV. Characteristics of X ray findings were not reviewed to determine if these patients fit ARDS criteria prior to transition, but the mean P:F ratio of 162 suggests that the majority of these patients were transitioned due to this clinical state.

Once the preserved oxygenation benefits of APRV have been established, we sought to determine potential detrimental effects on

Table 1
Patient Characteristics.

Characteristic	Value
Age (years)	40 +/− 17.2
Gender	
Male	87%
Female	13%
Admit GCS	3 (3–5)
Mortality	40%
Injury severity (ISS)	33.4 +/− 13.4
AIS head	4.1 +/− 0.9
AIS chest	3 (2–3)
ICU LOS (Days)	18 (7–22)
Hospital LOS (Days)	23 (7–28)
Epidural hematoma	27%
Subdural hematoma	47%
Subarachnoid hematoma	53%
Intraparenchymal hematoma	33%
Intraventricular hematoma	33%

Patient and injury characteristics. Normally distributed continuous variables are presented as mean +/− SD. Non-normally distributed continuous variables are presented as median and interquartile range.

Table 2
Ventilation Measurements Before and After Transition.

Characteristic	Before Transition	After Transition
Peak pressure (cm H2O)	35.3 +/− 7.2	
Plateau pressure (cm H2O)	25.6 +/− 5.5	
Static compliance (ml/cm H2O)	22.9 +/− 5.6	
Dynamic compliance (ml/cm H2O)	16.5 +/− 4.2	
PEEP (cm H2O)	10.3 +/− 3.3	
Time high (*sec*)		4.08 +/− 0.54
Pressure high (cm H2O)		31.6 +/− 5.5
Time low (sec)		0.79 +/− 0.12
Pressure low (cm H2O)		0 +/− 0
Auto PEEP (cm H2O)		10.8 +/− 4.4

Ventilator characteristics presented as mean +/− SD.

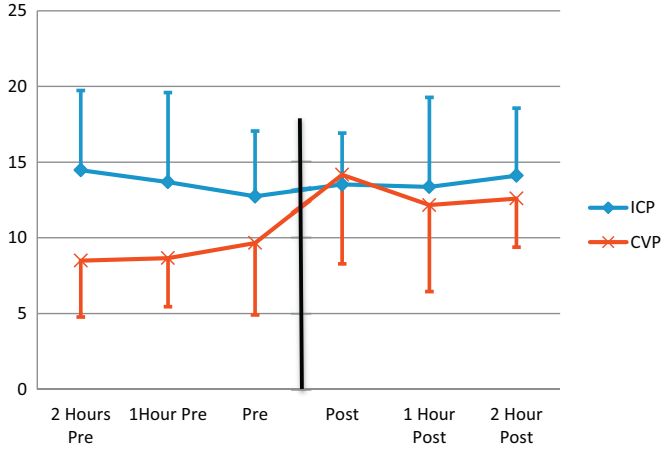

Fig. 1. ICP and CVP before and after transition to APRV.

ICP. CVP was elevated in patients following transition to APRV with a statistically significant difference. Importantly, however, ICP, CPP, and MAP were unchanged between the two groups. This suggests that the theoretical effect of higher CVPs contributing to venous congestion and elevated ICP based on the Monroe-Kellie hypothesis is not observed clinically. The same phenomenon has been observed in a porcine model in which increasing levels of PEEP led to decreased CVP but no change in ICP [8]. A transcranial doppler study demonstrated that statistically significant increases ICPs are not observed with increased PEEP if cerebral autoregulation and vasodilation are preserved. It was noted that any decrease in CPP was associated with decreased MAP, rather than an increase in ICP. [9] Others have suggested that the effect of PEEP on ICP is related to the effect of PEEP on aveoli dynamics. When PEEP was associated with increased alveolar recruitment as seen in ARDS there was no effect on ICP, whereas more compliant lungs in which PEEP led to alveolar hyperinflation associated with increased PaCO2 levels, there was an increase in ICP [10]. Caricato and colleagues examined the effects of increasing positive end-expiratory pressure (PEEP) on cerebral hemodynamics between patients having normal and low airway compliance (Crs). They found that in patients with normal Crs increasing PEEP significantly increased central venous pressure (CVP) and jugular venous pressure (JVP), and decreased MAP and CPP, although there were no differences in ICP or cerebral compliance as PEEP was increased in either group. [11] While the lack of an effect on ICP with elevated CVPs may also be seen in normal to high compliance patients, this has not been studied in TBI patients.

Additional research in TBI patients with normal to high airway compliance may identify an inflection point at which a transition to APRV remains safe. In the 19 transitions analyzed in our study, 4 were associated with ICP's >20 mmHg, although the number of ICP elevations >20/h on mode of ventilation was not statistically different. This is in contrast to the study performed by Fletcher et all in which ICP was noted to significantly decrease following a transition to APRV. We thus conclude that in patients with TBI and low airway compliance, APRV did not result in significantly increased ICP.

There are several limitations to this study. The sample size is small, so it may be underpowered to detect certain differences in hemodynamics changes before and after transition to APRV. It is a retrospective review and further research into the safety of APRV in TBI patients will need to be conducted in a randomized prospective fashion. It includes only patients with low airway compliance, who have been shown to be more resilient to changes in mean airway pressures. Patients with increased compliance may experience significant changes in hemodynamic parameters. The findings of this manuscript can not be applied universally to all patients. Additionally, patients with intracranial bleeds that are not the result of traumatic injury have the same narrow ICP goals that can be affected by other hemodynamic alterations, and may also be in need of advanced modes of mechanical ventilation. Similar research into this patient population is warranted.

5. Conclusions

Airway pressure release ventilation appears to be a safe mode of advanced mechanical ventilation to achieve improved oxygenation in patients with traumatic brain injury with low lung compliance.

Table 3
Changes in ICU Measurements Before and After Transition to APRV

Characteristic	Before Transition	After Transition	p value
Central venous pressure	**9.7 +/− 4.8**	**14.2 +/− 5.9**	**0.041**
Mean arterial pressure	87.2 +/− 12.8	86.8 +/− 14.5	0.884
Heart rate	96.3 +/− 22.1	96.3 +/− 23.8	0.989
ICP	12.7 +/− 4.3	13.5 +/− 3.4	0.356
Cerebral perfusion pressure	74.5 +/− 11.6	73.3 +/− 14.0	0.672
Minute ventilation	**13.2 +/− 2.9**	**9.8 +/− 2.3**	**<0.001**
Tidal volume	**567 +/− 127**	**699 +/− 112**	**0.001**
Temperature (C)	37.5 +/− 1.0	37.7 +/− 0.9	0.586
FiO2	0.61 +/− 0.15	0.71 +/− 0.23	0.943
pH	7.36 +/− 0.08	7.38 +/− 0.08	0.441
CO2	41.0 +/− 8.1	41.4 +/− 8.4	0.891
pAO2	**100.3 +/− 38.1**	**138.2 +/− 49.0**	**<0.001**
P:F ratio	**162.1 +/− 91.8**	**221.9 +/− 116.4**	**0.035**
Rate of ICP spikes (ICP > 20/hours of ventilation)	0.067 (0.018–0.217)	0.025 (0.0–0.128)	0.332

Physiologic characteristics before and after transition to APRV. Normally distributed continuous variables are presented as mean +/− SD. Non-normally distributed continuous variables are presented as median and interquartile range.
Bold data is significantly different p <0.050.

References

[1] Stock MC, Downs JB, Frolicher DA. Airway pressure release ventilation. LWW 1987.
[2] Daoud EG, Farag HL, Chatburn RL. Airway pressure release ventilation: what do we know? Respir Care 2012;57(2):282–92.
[3] Mireles-Cabodevila E, Kacmarek RM. Should airway pressure release ventilation be the primary mode in ARDS? Respir Care 2016;61(6):761–73.
[4] Habashi NM. Other approaches to open-lung ventilation: airway pressure release ventilation. Crit Care Med 2005;33(3) [S228-S40].
[5] Marik PE, Young A, Sibole S, Levitov A. The effect of APRV ventilation on ICP and cerebral hemodynamics. Neurocrit Care 2012;17(2):219–23.
[6] Salim A, Miller K, Dangleben D, Cipolle M, Pasquale M. High-frequency percussive ventilation: an alternative mode of ventilation for head-injured patients with adult respiratory distress syndrome. J Trauma Acute Care Surg 2004;57(3):542–6.
[7] Fletcher JJ, Wilson TJ, Rajajee V, Davidson SB, Walsh JC. Changes in therapeutic intensity level following airway pressure release ventilation in severe traumatic brain injury. J Intensive Care Med 2018 Mar;33(3):196–202.
[8] Muench E, Bauhuf C, Roth H, Horn P, Phillips M, Marquetant N, et al. Effects of positive end-expiratory pressure on regional cerebral blood flow, intracranial pressure, and brain tissue oxygenation. Crit Care Med 2005;33(10):2367–72.
[9] Georgiadis D, Schwarz S, Baumgartner R, Veltkamp R, Schwab S. Influence of positive end-expiratory pressure on intracranial pressure and cerebral perfusion pressure in patients with acute stroke. Stroke 2001;32(9):2088–92.
[10] Mascia L, Grasso S, Fiore T, Bruno F, Berardino M, Ducati A. Cerebro-pulmonary interactions during the application of low levels of positive end-expiratory pressure. Intensive Care Med 2005;31(3):373–9.
[11] Caricato A, Conti G, Della Corte F, Mancino A, Santilli F, Sandroni C, et al. Effects of PEEP on the intracranial system of patients with head injury and subarachnoid hemorrhage: the role of respiratory system compliance. J Trauma Acute Care Surg 2005;58(3):571–6.