Journal of Critical Care xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Effects of positive end-expiratory pressure on brain tissue oxygen pressure of severe traumatic brain injury patients with acute respiratory distress syndrome: A pilot study

Sérgio Nogueira Nemer, PT, PhD [a,b,c,*], Jefferson B. Caldeira, PT, MsC [a,c], Ricardo G. Santos, PT [a], Bruno L. Guimarães, PT [a], João Márcio Garcia, MD, PhD [a], Darwin Prado, MD [a], Ricardo T. Silva, MD [a], Leandro M. Azeredo, PT, MsC [b], Eduardo R. Faria, PT [a], Paulo Cesar P. Souza, MD [a]

[a] Complexo Hospitalar de Niterói. Rua La Salle 12, Centro, Niterói, Rio de Janeiro, CEP: 24020-090, Brazil
[b] Hospital da Polícia Militar de Niterói. Rua Martins Torres 245, Santa Rosa, Niterói, Rio de Janeiro, CEP: 24240-705, Brazil
[c] Universidade UNIGRANRIO. Rua José de Souza Herdy 1160, Jardim Vinte e Cinco de Agosto, Duque de Caxias, CEP: 25071-202, Brazil

ARTICLE INFO

Keywords:
Mechanical ventilation
Acute respiratory distress syndrome
Brain injury

ABSTRACT

Purpose: To verify whether high positive end-expiratory pressure levels can increase brain tissue oxygen pressure, and also their effects on pulse oxygen saturation, intracranial pressure, and cerebral perfusion pressure.
Material and Methods: Twenty traumatic brain injury patients with acute respiratory distress syndrome were submitted to positive end-expiratory pressure levels of 5, 10, and 15 cm H_2O progressively. The 3 positive end-expiratory pressure levels were used during 20 minutes for each one, whereas brain tissue oxygen pressure, oxygen saturation, intracranial pressure, and cerebral perfusion pressure were recorded.
Results: Brain tissue oxygen pressure and oxygen saturation increased significantly with increasing positive end-expiratory pressure from 5 to 10 and from 10 to 15 cm H_2O ($P = .0001$ and $P = .0001$ respectively). Intracranial pressure and cerebral perfusion pressure did not differ significantly with increasing positive end-expiratory pressure from 5 to 10 and from 10 to 15 cm H_2O ($P = .16$ and $P = .79$ respectively).
Conclusions: High positive end-expiratory pressure levels increased brain tissue oxygen pressure and oxygen saturation, without increase in intracranial pressure or decrease in cerebral perfusion pressure. High positive end-expiratory pressure levels can be used in severe traumatic brain injury patients with acute respiratory distress syndrome as a safe alternative to improve brain oxygenation.

1. Introduction

Traumatic brain injury (TBI) is the major cause of death and morbidity in young and adult people [1,2]. The 6-month mortality is higher in patients with Glasgow Coma Scale (GCS) between 3 and 6 and in those who are 80 years or older [3]. TBI is classified as mild (GCS scores of 13-15), moderate (GCS scores of 9-12) and severe (GCS scores of 3-8) [4]. Mortality is about 80% in patients with severe TBI [4]. Although secondary insults are more commonly treatable and often preventable, the secondary brain injury is a strong predictor of poor outcome and mortality, hypoxia and hypotension being the main causes [5]. Hypoxia (Pao_2 <60 mm Hg) can increase cerebral blood volume and intracranial pressure (ICP) and also contributes to brain ischemia [2,5]. Advances in monitoring such as brain tissue oxygen pressure ($PbrO_2$) can decrease the frequency and intensity of these episodes [5].

Acute respiratory distress syndrome (ARDS) is a devastating clinical syndrome that affects both medical and surgical patients [6]. The ratio of the partial pressure of oxygen to the inspired fraction of oxygen (Pao_2/Fio_2 ratio or P/F ratio) is the main parameter observed in patients with ARDS to assess hypoxemia, being used since 1988 by Murray Definition [7], until today, by Berlin Definition [8].

The development of ARDS in severe TBI patients is a bad combination, mainly if P/F ratio <100 mm Hg and ICP >20 mm Hg. ARDS occurs in 20% to 25% of patients with brain injury and it is an independent predictor of poor outcome [9]. The main ventilatory strategies used in ARDS patients, as low tidal volumes, high positive end-expiratory pressure (PEEP) levels, prone position and recruitment maneuvers are at least limited in TBI. From an optimistic point of view, at least one of the causes of secondary brain injury is present in severe TBI patients with ARDS: the hypoxemia. Being more realistic, we can easily observe other causes of secondary brain injury in severe TBI patients with ARDS, such as hypotension and hyperthermia [5]. Hypercapnia, frequently observed in ARDS patients can easily increase ICP and worsen the outcomes too. If it is difficult to ventilate an ARDS patient, ventilating a severe TBI patient with severe ARDS can be a challenge. $PbrO_2$ is frequently used in severe TBI patients to assess tissue oxygenation [10]. According to Brain Trauma Foundation [2], several studies suggested hyperoxia to increase $PbrO_2$. On the other hand, hyperoxia in the first 24 hours of intensive care unit admission after moderate-to-

* Corresponding author.
E-mail address: snnemer@gmail.com (S.N. Nemer).

http://dx.doi.org/10.1016/j.jcrc.2015.07.019
0883-9441/

severe TBI is not predictive on 6-month mortality [3]. As high F_{IO_2} levels can be deleterious and some patients with severe TBI and severe ARDS are already ventilated with F_{IO_2} in 100%, other alternative, and also our hypothesis is that high PEEP levels can increase $PbrO_2$. Therefore, the primary aim of this study is to verify the effects of PEEP on $PbrO_2$ and, as secondary aim, their effects on pulse oxygen saturation (Spo_2), ICP, and cerebral perfusion pressure (CPP).

2. Material and methods

This was a prospective study conducted between February 2007 to February 2014 in an Intensive Neurological Unit of Complexo Hospitalar de Niterói (Rio de Janeiro, Brazil), with a total of 12 beds. It was approved by the Ethics Committee of Unigranrio University (Rio de Janeiro, Brazil) and registered under number 06700313.0.0000.5283. Only patients who developed ARDS in the first week after TBI and were monitored by $PbrO_2$ were included. Until June 2012, the diagnostic of ARDS was based on American-European Consensus Conference [11] and after that, according to Berlin Definition [8].

For ethical and safe reasons, our exclusion criteria were as follows: patients younger than 18 or older than 80 years, brain death, presence of decompressive craniectomy, heart rate >120 bpm, ICP >20 mm Hg, CPP <60 mm Hg and $PbrO_2$ <15 mm Hg [2]. All patients received ICP measurement by ventricular catheter and remained with close external ventricular drain during the different PEEP levels. The Camino MPM-1 (Integra Neuroscience, Plainsboro, NJ) monitor was used to measure ICP, whereas $PbrO_2$ was monitored through the Licox device (Integra Neuroscience, Plainsboro, NJ) [2].

During the study, all patients were deeply sedated by continuous infusion of Midazolam and Fentanyl to keep RASS (Richmond Agitation-Sedation Scale) in −5. If necessary, atracurium or pancuronium infusions were used to paralyze patients who remained in asynchrony with mechanical ventilation. All patients were maintained at 30° head-up position during mechanical ventilation period. F_{IO_2} was adjusted to keep Spo_2 at ≥96%. During the study, all patients were ventilated on volume control ventilation. Tidal volume was adjusted to reach 6 to 7 mL/ideal body weight. Respiratory rate was adjusted between 15 and 25 to keep $Paco_2$ at around 35 to 40 mm Hg. Inspiratory to expiratory ratio was maintained at 1:2. Aiming to observe the evaluated parameters during the 3 PEEP levels, this one was changed from the previous value to 5 cm H_2O, 10 cm H_2O, and 15 cm H_2O, progressively. Aiming to avoid cyclic opening and alveolar collapse and according to animal study [12], we use incremental PEEP levels instead of randomized PEEP levels. Each PEEP level was kept for 20 minutes. During the 3 PEEP levels, all patients were kept without any change on ventilator parameters whereas the following parameters were recorded: ICP, CPP, $PbrO_2$, and Spo_2. In the case of 15 cm H_2O of PEEP resulting in a decrease of mean arterial pressure (MAP), infusion of norepinephrine was adopted to increase MAP back to baseline values (at least >80 mm Hg). In the case of ICP >20 mm Hg, CPP <60 mm Hg, $PbrO_2$ <15 mm Hg [2], or any intercurrence, the study was stopped and PEEP returned to the initial value (around 10 cm H_2O). In the case of CPP >60 mm Hg and ICP <20 mm Hg, the PEEP level that remained the highest in $PbrO_2$ was adopted after the procedures. The ventilators used were the Nellcor Puritan Bennet 840 (Hennef, Germany) and Servo-s or Servo-i (Maquet Critical Care, Solona, Sweden).

3. Statistical analysis

Analysis of variance for repeated measures with logarithmic transformation (natural log) according to Kolmogorov-Smirnov Test was used to verify changes on $PbrO_2$, ICP, CPP, and Spo_2 during the three PEEP levels. Bonferroni multiple comparisons test (adjusted for the three PEEP levels) was used to identify which evaluations differ significantly. The $P < .05$ was considered statistically significant. Statistical analyzes were performed using SAS 6.04 (SAS Institute, Inc, Cary, NC).

Table 1
Baseline characteristics of the evaluated patients

Baseline characteristics	Mean	SD	Median	Minimum	Maximum
Glasgow	5.85	1.13	6	3	8
Age; years	28.2	8.01	28	19	47
Pao_2/F_{IO_2} ratio	144.6	48.86	129	85	247
$PbrO_2$; mm Hg	26.4	6.87	24.5	18	40
ICP; mm Hg	8.9	4.21	8.5	2	16
CPP; mm Hg	92.1	10.04	95	77	110
Spo_2; %	94.95	2.39	94.5	91	99
F_{IO_2}; %	60.9	17.44	60	40	100
PEEP; cm H_2O	10.2	1.7	10	8	12

4. Results

Forty-one severe TBI patients were monitored by Licox device during the period between February 2007 and February 2014, but only 20 developed ARDS and were included in the study. There were 15 male (75%) and 5 female (25%) patients. Our patients already presented normal or high levels of MAP and CPP, even with minimum or no doses of vasoactive drugs. Therefore, no patient needed additional norepinephrine infusions to increase MAP or CPP even with the highest PEEP level (15 cm H_2O). Twelve patients had been paralyzed with atracurium before the study procedures, but the other 8 did not need to be paralyzed. No complication was observed during the entire study and no patient had to be excluded.

The great majority of patients had moderate ARDS (13 patients; 65%), while 5 (25%) had severe ARDS and only 2 (10%) had mild ARDS. The P/F ratio was 144.6 ± 48.86. Consequently, mean F_{IO_2} was higher than 60% (60.9 ± 17.44). Only 3 patients presented $PbrO_2$ < 20 mm Hg, but none presented values <18 mm Hg. The baseline characteristics of the patients are shown in Table 1.

$PbrO_2$ increased significantly with increasing PEEP from 5 to 10 cm H_2O (24.60 ± 6.84 to 26.55 ± 7.09; $P < .0001$) and from 10 to 15 cm H_2O (26.55 ± 7.09 to 29.05 ± 7.07; $P < .0001$). Changes in $PbrO_2$ are illustrated in Fig. 1. Spo_2 also increased significantly from 5 to 10 cm H_2O and from 10 to 15 cm H_2O ($P < .0001$ for both comparisons). On the other hand, ICP and CPP did not differ significantly with increasing PEEP from 5 to 10 and from 10 to 15 cm H_2O ($P = .16$ and $P = .79$, respectively). Changes in Spo_2, ICP and CPP are shown in Table 2. An example of a patient who presented its $PbrO_2$ increased from 20 mm Hg to 29 mm Hg, without any change on ICP, after an increment of PEEP to 10 cm H_2O and then to 15 cm H_2O is shown in Fig. 2. No patient needed a respiratory rate higher than 25 breaths per minute to keep $Paco_2$ between 35 and 40 mm Hg. As no patient presented a significant increase in ICP or decrease in CPP and presented increases in $PbrO_2$ and Spo_2 with the highest PEEP level, all patients (except the two mild ARDS) were ventilated with PEEP in 15 cm H_2O after the study. The 2 mild ARDS patients were ventilated with PEEP in 12 cm H_2O after the study.

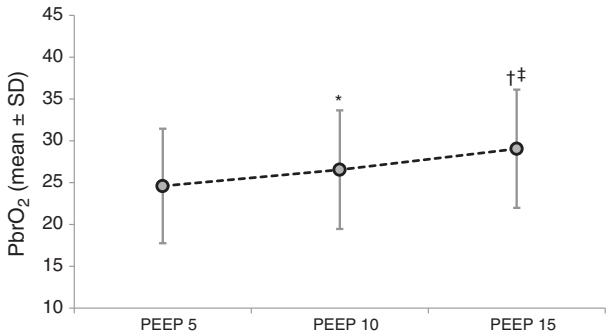

Fig. 1. Changes in $PbrO_2$ according to the three PEEP levels. Analysis of variance test for between-group comparison with Bonferroni post hoc. *$P < .0001$ *(PEEP 10 vs PEEP 5); †$P < .0001$ (PEEP 15 vs PEEP 15); ‡$P < .001$ (PEEP 15 vs PEEP 10).

Please cite this article as: Nemer SN, et al, Effects of positive end-expiratory pressure on brain tissue oxygen pressure of severe traumatic brain injury patients with acute r..., J Crit Care (2015), http://dx.doi.org/10.1016/j.jcrc.2015.07.019