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The impact of positive end-expiratory pressure on cerebral perfusion pressure in adult patients with hemorrhagic stroke

Repercussão da pressão positiva expiratória final na pressão de perfusão cerebral em pacientes adultos com acidente vascular hemorrágico

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ABSTRACT

Positive intrathoracic pressure may cause hemodynamic changes, which can be transmitted to the cranial compartment, changing intracranial pressure and cerebral perfusion pressure. This can be increased when high positive end-expiratory pressure values are used.

Objective: To measure the impact of different positive end-expiratory pressure levels on intracranial pressure, cerebral perfusion pressure and mean blood pressure.

Method: This study was conducted in a neurological intensive care unit and included 25 adult hemorrhagic stroke patients who were mechanically ventilated on airway pressure control mode. Patients were subjected to various positive end-expiratory values ranging between 0 and 14 cmH_2O. The order of these values were randomized, and the variables were assessed five minutes after each new positive end-expiratory pressure level was initiated.

Results: Incremental positive end-expiratory pressures led to increased intracranial pressure ($p < 0.001$), however, no statistically significant changes were observed in mean blood pressure or cerebral perfusion pressure.

Conclusion: In this population of patients with hemorrhagic stroke, positive end-expiratory pressure values up to 14 cmH_2O did not alter cerebral perfusion pressure or mean blood pressure. Increased intracranial pressures were noted, although these elevations were not clinically significant.

Keywords: Intracranial pressure; Positive-pressure respiration; Stroke

INTRODUCTION

The skull is a rigid, constant volume sphere containing cerebral tissues (1,400 mL), cerebrospinal fluid (150 mL) and blood (75 mL).[1-3] Preserved intracranial volume maintains normal intracranial pressure (ICP) values.[4,5] According to the Monro Kellie theory, volume changes in one compartment must be compensated by volume changes in a different compartment in order to maintain a constant intracranial volume and pressure.[1,6,7] The body is able to make physiological changes to maintain a normal ICP. However, when these coping mechanisms are exhausted, ICP increases.[4,6,8]

Intracranial hypertension (ICH) is common in intensive care unit (ICU) patients admitted for different reasons. These may include central nervous system or systemic conditions from traumatic, infective or metabolic causes.[7,9,10] ICH is currently defined as pressure values persistently above 20 mmHg.[1,11] Under normal conditions, the vascular cerebral resistance regu-

lation mechanisms are able to maintain constant blood flow under a wide range of cerebral perfusion pressures (CPP).[1,4,8] Failure of the regulating mechanisms will lead to reduced tissue perfusion and worsened ischemic cell injury.[1,4,8,12]

Monitoring of ICH patients should include continuous vital sign assessment and maintenance, with special attention to hypotension, hypoxia, brain edema, hemorrhage, herniation and hemodynamic changes. The effectiveness of the therapy should also be continually reassessed.[1,9]

Acute brain injury patients have a high likelihood of pulmonary involvement, leading to reduced arterial oxygen pressure (PaO_2) and carbonic gas (CO_2) retention, requiring mechanical ventilation assistance (MVA).[1,13-17] Approximately 20% of intracranial hemorrhage patients will eventually develop a respiratory infection, pulmonary edema and acute lung injury requiring more aggressive MVA aimed at reverting hypoxemia.[14] These developments are especially common in patients receiving positive end-expiratory pressure (PEEP).[18-24] MVA may impact hemodynamics,[25] leading to increased ICP and reduced CPP. This is because the compression of the alveolar capillary vessels by distended alveoli may lead to increased right-ventricular afterload, thus reducing the venous return. However, few articles assessing the impact of high PEEP values on ICP and CPP are available in the literature.[26-31] Higher PEEP values could be necessary, even in normal complacent patients, aimed at RFC (residual functional capacity) optimization after airway suction, as this procedure may lead to reduced tidal volume and pulmonary complacency on the pressure control mode.[32]

This study was designed to assess the effects of PEEP on ICP and CPP in adult patients during the acute phase after a hemorrhagic stroke (HS) without ICH.

METHODS

This was a prospective trial conducted at the neurological ICU of Real Hospital Português de Beneficência em Pernambuco, Brazil. This study was approved by the institution's ethics committee under the registration number #402. An informed consent form was signed by each patient's legal representative.

The inclusion criteria were adult patients with HS secondary to systemic arterial hypertension and invasive ventricular drainage and ICP monitoring catheter, without intracranial hypertension. Patients with intracranial hypertension (ICP > 20 mmHg), hemodynamic instability (MBP < 70 MMhG), and an SpO_2 < 90% were excluded. Patients could also be withdrawn from the study upon the request of their legal representative, however, all patients completed the study.

The study would be discontinued if during the protocol ICP increased above 20 mmHg, arterial blood pressure increased by 20 mmHg, SpO_2 dropped below 90%, respiratory rate (RR) was increased, or capnometry was above than 46 mmHg.

Orotracheally intubated patients referred from surgery, receiving manual AMBU ventilation, were adapted to a mechanical ventilator (Inter5, Intermed, São Paulo, Brazil) on pressure control mode when they arrived in the ICU. These patients were also equipped with an implanted ventricular catheter and their vital signs were monitored using a multi-parameter monitor (7000 Siemens). After 30 minutes of stabilization in the ICU, the patient was maintained at a 30º bed head elevation and the protocol was started to assess the impact of PEEP on ICP. To assess the pulmonary mechanics, the ventilation mode was changed to volume control with the following parameters: tidal volume (TV) = 8 mL/kg body weight, peak flow (PF) = 6 x volume minute, inspired O_2 fraction (FiO_2) = 40%, respiratory rate (RR) = 16 inspirations per minute (ipm), sensitivity = 1 cmH_2O. The following variables were monitored: ICP, blood pressure (BP), heart rate (HR), respiratory rate (RR), peak airway pressure (Pp), peripheral oxygen saturation (SpO_2), capnometry, and respiratory system plateau pressure (Ppl). A 3 second pause was used for measuring Ppl and the assessments were performed with PEPP = 5 cmH_2O.

During the assessment protocol, pressure control mode was used with the following ventilation parameters: Pp = 30 cmH_2O, inspiratory time: 1 second, FiO_2 = 40%, RR = 16 ipm, and sensitivity = 1 cmH_2O. PEEP ranged between 0 and 14 cmH_2O, using even values. To eliminate the likely physiological accommodation due to progressive PEEP increases, the orders of the PEEP values were randomized using one sealed envelope per patient. For each PEEP value, the patient was ventilated for five minutes and then ICP, BP, HR, CPP, RR, SpO_2 and capnometry were measured. The ICP monitoring catheter was kept closed for drainage and open for monitoring since the arrival from the surgery room, and only open for drainage if ICP increased above 20 mmHg.

For the purpose of ICP monitoring, the ventricular catheter was connected to a pressure transducer that was connected to the monitor. Blood pressure was in-

vasively controlled via radial artery puncture with the catheter connected to a pressure transducer that was connected to the monitor.

After the parameters were assessed with seven different PEEP values, ventilation mode was changed to volume control to reassess pulmonary mechanics with the initial parameters.

Statistical analysis

The results are expressed as mean ± standard deviation. The Kolmogorov-Smirnov test was used to assess the distribution of continuous variables. The Student's t test or ANOVA was used to evaluate pairwise repeated measures. The ANOVA-identified differences were examined using the Least Significant Difference (LSD) test. A 5% level was considered significant, with a β error of 20%. The data were analyzed using Excel 2000 and SPSS v8.0 software.

RESULTS

All patients included in this study complied with the protocol and no patients met the discontinuation criteria. The sample's characterization is shown in table 1.

HR, RR, SpO_2 and capnometry were not changed at any PEEP level, $p > 0.5$ (Table 2). ICP was significantly increased for the following PEEP values: 10, 12 and 14 cmH_2O as compared with 0 cmH_2O; 8, 10, 12 and 14 cmH_2O as compared with 2 cmH_2O; 8, 10, 12 and 14 cmH_2O as compared with 4 cmH_2O; 12 and 14 cmH_2O as compared with 6 cmH_2O; 12 and 14 cmH_2O as compared with 8 cmH_2O; and 12 and 14 cmH_2O as compared with 10 cmH_2O (Figure 1).

Table 3 shows CPP and MBP mean distributions as related to the different PEEP values. No statistically significant differences were identified for CPP and MBP means.

Table 1 – Patients' characteristics

Overall	N	%
Gender		
Female	7	28.0
Male	18	72.0
Age (64.9 ± 11.6 years)		
42 to 66	12	48.0
68 to 86	13	52.0
Disease		
Hemorrhagic stroke	25	100.0
ICU stay before the protocol	25 (up to one hour)	100.0
Time of orotracheal intubation	25 (up to 3 hours)	100.0
Reported systemic hypertension	25	100.0

ICU – intensive care unit.

Table 2 – Analysis of respiratory variables according to the positive end-expiratory pressure level

PEEP	RR*	SpO_2*	Capnometry*
0	16	99.1 ± 1.66	34.44 ± 1.08
2	16	98.8 ± 1.61	34.6 ± 1.0
4	16	99 ± 1.49	34.64 ± 0.95
6	16	98.9 ± 1.28	34.72 ± 0.89
8	16	99 ± 1.63	34.76 ± 0.83
10	16	99.2 ± 1.03	35 ± 0.7
12	16	99.4 ± 0.69	35.16 ± 0.68
14	16	99.5 ± 0.84	35.28 ± 0.73

*$p > 0.05$. PEEP – positive end-expiratory pressure; RR – respiratory rate; SpO_2 – peripheral oxygen saturation.

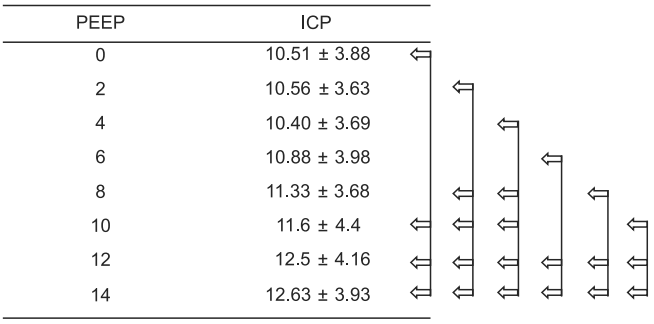

Figure 1 – Assessment of intracranial pressure according to the positive end-expiratory pressure levels.

PEEP – positive end-expiratory pressure; ICP – intracranial pressure. ICP pressure was different between the first arrow and other arrows in the same line. $p < 0.05$.

Table 3 – Analysis of hemodynamic variables and cerebral perfusion pressures according to the positive end-expiratory pressure level

PEEP	MBP*	CPP**	HR *
0	100.6 ± 16.2	90.1 ± 17.5	78 ± 11.63
2	99.4 ± 15.6	88.9 ± 16.1	77.63 ± 11.47
4	99.0 ± 13.9	88.6 ± 15.0	79 ± 11.84
6	98.1 ± 14.1	87.2 ± 14.4	77.81 ± 10.79
8	98.2 ± 15.4	86.9 ± 15.7	76.54 ± 10.73
10	98.3 ± 21.7	86.7 ± 22.3	78.09 ± 11.86
12	101.0 ± 15.6	88.8 ± 16.4	78.72 ± 11.08
14	100.5 ± 16.8	88.0 ±17.0	77 ± 12.19

*$p = 0.266$; **$p = 0.588$. PEEP – positive end-expiratory pressure; MBP – mean blood pressure; CPP – cerebral perfusion pressure; HR – heart rate.

A comparison between initial and final mean static respiratory system complacency, with a PEEP of 5 cmH_2O, showed a significant increase from the initial value of 49.6 ± 11.2 to 61.4 ± 14.2, $p < 0.001$.

DISCUSSION

Based on the results, we conclude that in this population of patients with respiratory system complacency within the physiological range, higher PEEP values significantly increased ICP. However, this finding lacks clinical relevance because even the highest PEEP value tested was below the 20 mmHg boundary. MBP and CPP were not changed. It is interesting to note that incremental increases in PEEP augment final complacency, as compared to the initial values, in a statistically significant fashion.

Theoretically, PEEP values above 10 cmH_2O could be harmful to the intracranial compartment because they may reduce systemic venous return.[26] This transmission of PEEP into the thoracic compartment is influenced by the chest wall, the lung's properties and the patient's hemodynamics. A study conducted by Chapin et al.[27] showed that in the setting of low chest wall complacency, PEEP increases the intrathoracic pressure with possible meaningful hemodynamic changes. However, this would not be seen with reduced pulmonary complacency.

How was dissipated the increased intrapulmonary pressure, with PEEP values ranging between 0 and 14 cmH_2O, not causing clinically meaningful ICP increase? Apparently, intrathoracic pressure is not directly transmitted into the cerebral compartment, given that respiratory system complacency, hemodynamic stability, cerebral elasticity and the actual PEEP values could also influence this relationship. Therefore, the sum of these factors will determine the transmission of alveolar pressure into pleural pressure, which is reflected in the hemodynamic system. Cuypers et al.[28] have shown that increased central venous pressure in cats only leads to a transient increase in ICP, suggesting that increased right atrium pressure would not be a determinant of increased ICP. Thus, reduced venous return caused by alveolar capillary vessel compression due to PEEP would not be sufficient enough to increase ICP.

Our results regarding the impact of PEEP on ICP are different from those described by Aidinis et al.,[29] who assessed induced lung injury in animals. The data from our study are partially different from those of Apuzzo et al.[30] and Burchiel et al.,[31] but were similar to the findings in normal cerebral elasticity patients. In contrast to the conclusions by Huynh et al.,[33] our results showed no increase in CPP.

Similar to Cooper et al.,[34] whose study design was similar to ours, we observed increases in ICP that were not clinically meaningful. This differed from the findings of Georgiadis et al.,[35] who found no ICP increase.

Our patients were laying in supine decubitus with a 30º bed head elevation. In this position, the chest is lower than the intracranial compartment, easing the venous return, preventing excessive increases in ICP. Schwarz et al.[36] assessed the effects of positioning the head above the chest in hemorrhagic stroke patients and observed that a 30º bed head elevation leads to reduced ICP. Toung et al.[37] used an animal study to evaluate the effects of bed head elevation on the impact of PEEP on cerebrospinal fluid pressure. The results showed that the ICP was not changed when PEEP values of 15 cmH_2O were used. A raised bed head is likely to have influenced the lack of increased ICP in our study.

In assessing the impact of PEEP on CPP, our results corroborate the findings of McGuire et al.,[38] who found no CPP changes during the use of high PEEP values. Considering that the heart is contained within a pressurized chamber, during MVA the positive intrathoracic pressure leads to a reduced left ventricular transmural pressure. This increases the ejection volume, contributing to stable CPP even with increased ICP.[39]

Our results agree with previous studies[35-38] with respect to the lack of MBP changes secondary to increased PEEP. Positive intrathoracic pressure may reduce the cardiac output due to reduced venous return,[40] however, this would be minimized by the improved left ventricle function, explaining MBP stability.

Static complacency, below physiological values, minimizes negative PEEP cardiovascular system effects.[27] Our patients had static complacency below physiological values and when initial and final complacency values were compared, a significant increase was observed. This suggests that previously collapsed or low-volume alveoli were recruited, therefore dissipating the pressure that would be transmitted to the cardiovascular system. This would explain why we did not appreciate any clinically meaningful he-

modynamic effects. Based on our study design, the patients were ventilated on pressure control mode, limiting the maximal respiratory system pressure. Even when increasing PEEP, Pp was not changed. This finding was different from that of other studies,[29,30] with dissimilar results showing increased maximal respiratory system pressure upon PEEP increase.

As Pp was limited, PEEP increases would reduce the pressure delta and TV, which could result in CO_2 retention. However, our results showed no statistically significant capnographic changes. Our hypothesis is that this is due to the short time in each PEEP value, which would be insufficient to cause changes. Another possible explanation is that PEEP increases improved the complacency and may have caused increased TV.

A limitation of our study is that the values were not directly obtained from blood gas measurements, but were indirectly monitored by capnometry and SpO_2. In addition, we did not assess the tidal volume to the patient during the protocol.

CONCLUSION

Our findings show that, in our population sample, the use of high PEEP values caused no clinically meaningful changes to ICP, CPP and MBP. Our results suggest that in patients with acute lung injury or respiratory distress syndrome, PEEP values up to 14 cmH_2O could be used for gas exchange optimization, and may also prove beneficial in improving these patients' residual capacity following suction or ventilator circuit disconnection. However, additional longer and multicenter studies would be useful in confirming these findings.

RESUMO

A pressão positiva intratorácica pode levar a alterações hemodinâmicas com repercussão no compartimento intracraniano, alterando a pressão intracraniana e a pressão de perfusão cerebral. Esse efeito pode se tornar mais intenso quando utilizados elevados valores de pressão positiva expiratória final.

Objetivo: Medir o impacto que diferentes valores de pressão positiva expiratória final causam na pressão intracraniana, na pressão de perfusão cerebral e pressão arterial média.

Método: O estudo foi desenvolvido em uma unidade de terapia intensiva neurológica envolvendo 25 pacientes adultos com acidente vascular cerebral hemorrágico, ventilados mecanicamente no modo com controle pressórico de vias aéreas. Foram instituídos valores de pressão positiva expiratória final variando de 0 a 14 cmH_2O, de forma aleatória através de sorteio, utilizando valores pares. A monitorização das variáveis estudadas ocorreu após cinco minutos em cada patamar de pressão positiva expiratória final.

Resultados: O incremento da pressão positiva expiratória final aumentou a pressão intracraniana, ($p < 0,001$) sem causar alteração estatisticamente significativa na pressão arterial média ou na pressão de perfusão cerebral.

Conclusão: Na população estudada, de pacientes com acidente vascular cerebral hemorrágico, os achados mostraram que valores de pressão positiva expiratória final até 14 cmH_2O, não alteram a pressão de perfusão cerebral e a pressão arterial média, aumentando a pressão intracraniana, porém sem relevância clínica.

Descritores: Pressão intracraniana; Pressão positiva expiratória final; Acidente cerebral vascular

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