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Effects of expiratory tracheal gas insufflation in patients with severe head trauma and acute lung injury

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Abstract *Objective:* This study analyzed the effect of phasic tracheal gas insufflation at mid- to end-expiration in patients with severe head trauma and acute lung injury (ALI)/ acute respiratory distress syndrome (ARDS). *Design and setting:* A prospective interventional study in a 16-bed intensive care unit. *Patients:* Seven patients with severe head trauma (Glasgow Coma Scale <9) and ALI/ARDS. *Interventions:* Patients were ventilated in assist/control mode with a ventilatory strategy providing adequate oxygenation (PaO_2 >70 mmHg) and normocapnia ($PaCO_2$ between 35–40 mmHg). Mid to end expiratory tracheal gas insufflation at 8 l/min flow rate was delivered for 90 min while normocapnia was maintained by simultaneous reductions in tidal volume. We measured (hemodynamics, oxygenation, lung mechanics, and cerebral parameters) in basal situation and during and after tracheal insufflation. *Measurements and results:* Tracheal gas insufflation allowed a significant decrease in tidal volume from 9.1 to 7.2 ml/kg, with associated reduction in driving pressure (plateau pressure minus positive end-expiratory pressure, PEEP) from 18.1 to 13.2 cmH_2O. Total PEEP increased from 9.3 to 12.7 cmH_2O due to the generation of lung hyperinflation. Oxygenation improved slightly during tracheal gas insufflation, and this improvement remained after stopping tracheal insufflation. No changes in hemodynamic or cerebral parameters were observed during the study. *Conclusions:* In patients with severe head trauma and ALI receiving mechanical ventilation, expiratory tracheal gas insufflation allowed the targeted arterial PCO_2 level to be maintained together with a substantial reduction in tidal volume.

Keywords Severe head trauma · Acute lung injury · Tracheal gas insufflation · Ventilator-induced lung injury · Ventilator protective strategy · Cerebral-lung interactions

Introduction

Patients with severe head trauma are at high risk of developing acute lung injury (ALI). ALI is present in 20% of patients with severe traumatic brain injury (Glasgow Coma Scale, GCS, <9), and these ALI patients are three times more likely to survive in a vegetative state or to die [1]. Guidelines for mechanical ventilation in head trauma patients suggest that ventilator settings should be adjusted to maintain $PaCO_2$ at the lower range of normocapnia ($PaCO_2$ between 35–37 mmHg), while PaO_2 should be higher than 70 mmHg to ensure adequate cerebral oxygenation [2, 3]. Hypercapnia attenuates or abolishes brain autoregulation, induces cerebral vasodilatation, and increases intracranial pressure by CO_2-mediated alteration of brain extracellular pH and its effect on cerebral vascular tone [4]. Consequently, permissive hypercapnia is

contraindicated in patients with severe head trauma [5, 6, 7].

Mechanical ventilation can induce and perpetuate acute lung injury by overdistention and cyclic collapse and reopening of alveolar units with each tidal breath [8, 9]. Injurious mechanical ventilation in patients with ALI might promote an increase in cytokine levels in the lung and in the systemic circulation, but this response can be attenuated by a protective ventilatory strategy [10]. In patients diagnosed with acute respiratory distress syndrome (ARDS) Amato et al. [11] and the ARDS network trial [12] demonstrated that a protective ventilatory strategy with low tidal volumes (V_T) and limited airway pressures improved survival. In the former study [11] severity of illness scores and inspiratory driving pressure, i.e., the difference between plateau pressure and total positive end-expiratory pressure (PEEP; the sum of external PEEP and autoPEEP), were predictors of mortality. In the latter [12], relative normocapnia was a characteristic feature both of control and treatment groups.

Tracheal gas insufflation (TGI) is an adjunct to mechanical ventilation that allows ventilation with low V_T while carbon dioxide is satisfactorily cleared. Several studies have shown that TGI can be used either to decrease $PaCO_2$ in the setting of hypercapnia or to maintain isocapnia while V_T is decreased [13, 14, 15]. Patients with head trauma and ALI/ARDS need aggressive treatment to maintain normal intracranial pressure (ICP). This may necessitate the use of relatively high V_T and minute ventilation with high airway pressures. In this setting TGI can be a useful adjunct to lower V_T while maintaining $PaCO_2$ constant. However, the usefulness of TGI in head trauma patients has only been evaluated in anecdotal case reports [16, 17].

The objective of this study was to analyze the effect of phasic TGI at mid- to end-expiration in patients with severe head trauma and ALI/ARDS. We hypothesized that in these patients TGI allows a more protective ventilatory strategy at normal values of $PaCO_2$ without compromising intracranial pressure, cerebral perfusion pressure, or cerebral circulation. Part of this work has been previously published as an abstract in the 15th Annual Congress of the ESICM in Barcelona, Spain, on 29 September–2 October 2002 [18].

Material and methods

Patients

We prospectively studied seven patients aged between 28 and 81 years (mean 55±17 years) admitted to the Critical Care Center of our University Hospital for severe head trauma, defined as a GCS less than 9. Patient demographic and clinical characteristics are shown in Table 1. The approval of the hospital's ethics and clinical research committees was granted, and written informed consent was obtained from authorized relatives of patients prior to the study. We enrolled mechanically ventilated patients who developed ALI in the acute phase of head trauma, based on the criteria of the American-European Consensus Conference on Acute Respiratory Distress Syndrome (ARDS) [19] with a lung injury score (LIS) [20] mean 2.8±0.5, range from 2 to 3.5. Cerebral monitoring included intracranial pressure, cerebral metabolism, and cerebral blood velocity. Intracranial pressure was performed using the OLM intracranial pressure monitoring kit with a Camino parenchymal pressure-tipped catheter (Integra Neurosciences-Camino, San Diego, Calif., USA) and MPM-1 monitoring system of Neurocare-Group-Camino (Integra Neurosciences, Plainsboro, N.J., USA). Cerebral metabolism was estimated by continuous fiberoptic jugular venous oximetry using a flow-directed thermodilution fiberoptic catheter (Opticath catheter of 5.5 F) placed in the right jugular vein (Oximetrix SO_2 systems, Abbot Critical Care Systems, North Chicago, Ill., USA) and registered with the Oxymetrix3-SO_2/CO_2 computer (Abbot). For the determination of jugular bulb oxygen saturation we calibrated each measurement in vivo by drawing a blood sample from the tip of the catheter. Cerebral blood flow velocity spectrum was monitored by intermittent transcranial Doppler with the TC2-64 Transcranial Doppler System (EME, Überlingen. Germany). Transcranial Doppler measurements were performed in all patients by the same investigator and in the same temporal zone previously marked to avoid under or overestimations of repeated measurements. The mean bilateral middle cerebral artery velocity and pulsatility index were recorded [21].

Table 1 Clinical characteristics of the patients

Patient no.	Sex	Age (years)	Pulmonary diagnosis	Lung Injury Score	Head trauma diagnosis	Glasgow Coma Scale
1	M	57	Aspiration pneumonia	2.0	Subdural hematoma	7
2	F	59	Neurogenic edema	3.0	Traumatic subrachnoid hemorrhage	8
3	M	62	Ventilator-associated pneumonia	3.25	Traumatic subrachnoid hemorrhage, swelling	3
4	M	81	Aspiration pneumonia	2.5	Subdural hematoma	7
5	M	58	Aspiration pneumonia	2.75	Hemorrhagic contusion	8
6	M	41	Lung contusion	3.5	Traumatic subrachnoid hemorrhage; diffuse axonal injury	4
7	M	28	Ventilator-associated pneumonia	2.75	Diffuse axonal injury Swelling	3
Mean	–	55	–	2.8	–	5.7
SD	–	17	–	0.5	–	2.2

Protocol

Patients were orally intubated with a cuffed endotracheal tube with an internal diameter ranging from 8 to 9 mm and were ventilated in control mode with a constant square wave inspiratory flow by using a 900C Servo-ventilator (Siemens, Solna, Sweden). The study was performed 6.7±1.7 days after admission. Patients were deeply sedated with midazolam and morphine. Our neurological guidelines oriented ventilatory strategy included a tidal volume of 8–10 ml/kg of predicted body weight, a plateau pressure of 35 cmH$_2$O or lower, FIO$_2$ and PEEP to allow PaO$_2$ higher than 70 mmHg, and minute ventilation to maintain PaCO$_2$ values close to the lower range of normocapnia. Standard monitoring included heart rate, electrocardiography, and continuous noninvasive assessment of oxygen saturation by pulse oximetry (HPM1020 A. Palo Alto, Calif., USA). For the strict control of PaCO$_2$, patients had an indwelling, continuous arterial blood gas sensor, a Paratrend 7 FL multiparameter sensor (Diametrics Medical Incorporated, Roseville, Minn., USA) inserted via the radial artery and connected to the Trendcare satellite monitor (Diametrics Medical, Roseville, Minn., USA). The Paratrend catheter was also connected for continuous blood pressure monitoring using a pressure gauge transducer (HPM1006 A; Palo Alto, Calif., USA). For TGI an open-end catheter with multiple side ports was inserted within the endotracheal tube for intratracheal gas delivery, and was positioned 2 cm above the carina (checked radiographically). Airway pressure and airflow were measured with the devices built into the ventilator and recorded by a Vue-Link module. Plateau pressure was measured as the airway opening pressure after a 4-s occlusion at end-inspiration. Auto PEEP was calculated 2 sec after an end-expiratory occlusion (TGI flow was stopped during auto-PEEP measurement). Total PEEP was defined as external PEEP plus auto PEEP. Static compliance of the respiratory system was obtained by dividing the tidal volume by the difference between plateau pressure and the total PEEP. Hemodynamics, lung mechanics, oxygenation, and cerebral monitoring were obtained in basal situation after a 30-min stabilization period.

TGI with the same FIO$_2$ as that delivered by the ventilator was applied at 8 l/min in the mid- to end-expiratory phase using a prototype TGI controller (Valley Inspired Products, Burnsville, Minn., USA). The prototype controls TGI flow by monitoring airways flow with a pneumotachometer. TGI flow started at mid-expiration and stopped at the end of the ventilator expiratory time with the onset of inspiration. Immediately after initiation of the TGI period V$_T$ was gradually reduced to maintain isocapnia, and 90 min thereafter we collected data on hemodynamics, lung mechanics, oxygenation, and cerebral parameters. Afterwards TGI was stopped, and V$_T$ increased to the pre-TGI level. During the study the ventilatory frequency was kept constant. Data were again collected after a 90-min stabilization period. Safety criteria for stopping the protocol were a 20% increase in intracranial pressure or a 20% decrease in cerebral perfusion pressure (CPP). There were no complications related to TGI, and it was not necessary to interrupt the protocol in any patient due to clinical deterioration or significant variations in ICP or CPP.

Statistical analysis

All values are presented as mean ±SD. Statistical analysis was performed using a Wilcoxon nonparametric test. Significance was set at $p<0.05$.

Results

Effect of TGI on hemodynamics and gas exchange

Basic hemodynamic data (heart rate, mean systemic arterial pressure, and central venous pressure) were not different before, during, and after TGI (Table 2). PaO$_2$/FIO$_2$ improved from 151±45 mmHg in basal situation to 164±35 mmHg with TGI ($p=0.018$). After stopping TGI PaO$_2$/FIO$_2$ remained elevated at 174±34 mmHg ($p=0.027$). It is important to note that isocapnia was strictly maintained throughout the study as a part of the protocol (Table 2), as long as there were no changes in arterial pH.

Effect of TGI on respiratory system mechanics

Despite the reduction in V$_T$ during TGI no changes were observed in peak and plateau pressures or in static compliance of the respiratory system. All patients presented autoPEEP, which increased from 0.3±0.7 cmH$_2$O in basal situation to 3.7±1.5 cmH$_2$O during TGI ($p=0.018$) and, consequently, total PEEP significantly increased. Inspiratory driving pressure decreased from 18.1±3.4 to 13.2±2.1 cmH$_2$O with TGI ($p=0.018$) and returned to 16.7±3.5 cmH$_2$O after stopping TGI. Individual variations in inspiratory driving pressure are shown in Fig. 1. During TGI V$_T$ was significantly reduced from 9.1±0.8 to 7.2±0.7 ml/kg ($p=0.018$) and returned to the baseline level when TGI was withdrawn. Individual variations in V$_T$ are shown in Fig. 2. Table 3 summarizes respiratory system mechanics before, during, and after TGI.

Effect of TGI on cerebral parameters

Table 4 summarizes the cerebral parameters before, during, and after TGI. No significant changes were observed in the cerebral parameters before, during, or after TGI application except for a slight but statistically significant decrease in the pulsatility index of the right middle cerebral artery and an increase in the mean velocity of the

Table 2 Hemodynamic and gas exchange parameters before, during, and after tracheal gas insufflation

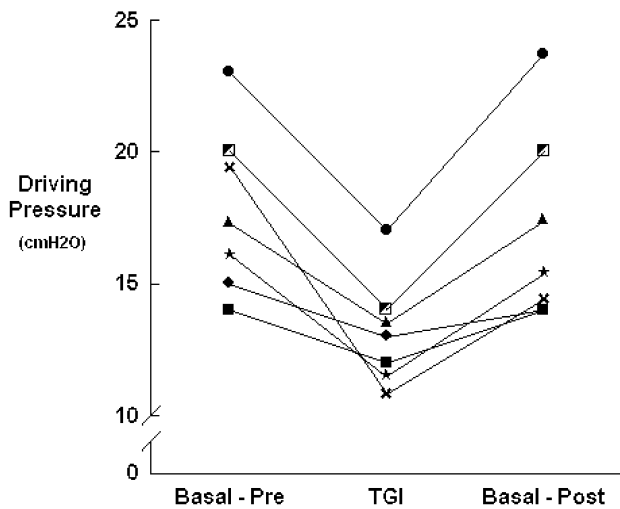|	Basal	TGI	Post-TGI
Heart rate (beats/min)	85±18	85±19	86±19
Mean arterial pressure (mmHg)	95±8	97±11	92±10
Central venous pressure (mmHg)	16±4	17±4	16±4
Arterial pH	7.43±0.03	7.41±0.03	7.42±0.03
PaCO$_2$ (mmHg)	36±1	36±2	36±2
PaO$_2$/FIO$_2$ (mmHg)	151±45	164±35*	174±34*

*$p\leq0.05$ vs. basal

Fig. 1 Individual airway driving pressure values in basal situation, during tracheal gas insufflation, and after tracheal gas insufflation was stopped. All patients showed a decrease in driving pressure during tracheal gas insufflation application that returned to the basal levels in the post-tracheal gas insufflation phase. *$p=0.018$
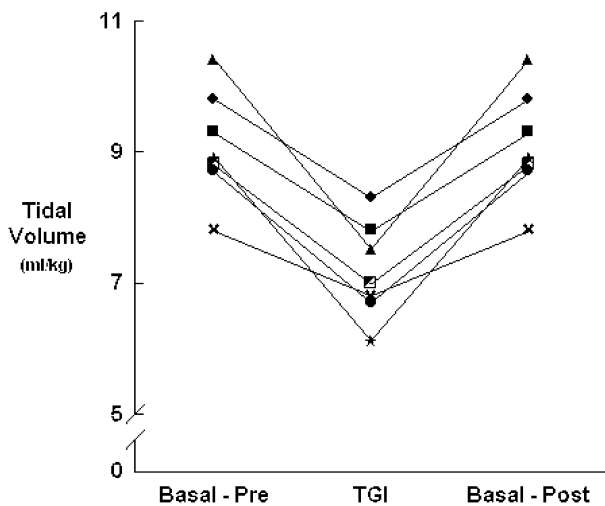

Fig. 2 Individual tidal volume values in ml/kg predicted body weight, before, during, and after the application of tracheal gas insufflation. There is a statistically significant reduction in tidal volume. This change was achieved in every patient. *$p=0.018$

left middle cerebral artery. Changes in ICP in none of the patients were statistically significant ($p=0.49$) and are shown in Fig. 3.

Discussion

The main findings of this study were: (a) Application of TGI in patients with ALI/ARDS and severe head trauma is feasible and allows a more protective ventilatory strategy, with lower V_T and lower inspiratory driving

Table 3 Lung mechanics before, during, and after tracheal gas insufflation

	Basal	TGI	Post-TGI
Airway peak pressure (cmH_2O)	41.4±5.8	37.5±3.3	40.1±5.1
Airway plateau pressure (cmH_2O)	27.4±4.7	26.1±2.5	26.4±3.7
Airway driving pressure (cmH_2O)	18.1±3.4	13.2±2.1*	16.7±3.5
AutoPEEP (cmH_2O)	0.3±0.7	3.7±1.5*	0.5±0.9
Total PEEP (cmH_2O)	9.3±2.8	12.7±3.4*	9.5±2.6
Respiratory system compliance (ml/cmH_2O)	33.9±7.6	35.3±7.1	36.8±8.5
Respiratory rate (breaths/min)	19.7±3.5	19.7±3.5	19.7±3.5
Tidal volume (ml/kg)	9.1±0.8	7.2±0.7*	9.1±0.8
Minute ventilation (l)	11.8±2.9	9.2±2.1*	11.7±3.0

*$p\leq0.05$ vs. basal

pressure, while maintaining $PaCO_2$ constant. (b) TGI has no short-term deleterious effects on hemodynamics and, more importantly, no deleterious effects on the cerebral parameters.

Rationale for using TGI in patients with head trauma

The best strategy of mechanical ventilation in patients with severe head trauma remains controversial. Current guidelines and reviews [2, 3] recommend adjusting the ventilator settings to maintain $PaCO_2$ close to 35 mmHg and PaO_2 higher than 70 mmHg. Abnormal levels of CO_2 have several complex physiological effects on cerebral circulation, and small changes in $PaCO_2$ could have several clinical manifestations. In this setting, hypoventilation and associated hypercapnia are formally contraindicated in patients with severe head trauma because of the risk of worsening intracranial hypertension related to the increase in cerebral blood flow induced by cerebral vasodilatation and increased systemic blood pressure [6, 7]. Experimental studies have demonstrated that hypercapnia reduces cerebral autoregulation, which is abolished by a further elevation, i.e., a $PaCO_2$ higher than 70 mmHg [4]. Despite the fact that respiratory acidosis rather than hypercapnia per se is the cause of these alterations, the acute development of hypoventilation in patients with brain injury can lead to an intracranial mass effect, compromised cerebral perfusion, and even brain herniation. On the other hand, the effects on outcome of long-term hyperventilation are uncertain. Muizelaar et al. [22] demonstrated that prolonged hyperventilation, with $PaCO_2$ of 25 mmHg, worsened the outcome of head-injured patients. Moreover, hypocapnia may also cause alterations in pulmonary capillary permeability and parenchymal lung injury [4, 23].

Ventilator-induced lung injury is related to traditional approaches to mechanical ventilation that use high V_T and

Table 4 Cerebral parameters before, during, and after tracheal gas insufflation

	Basal	TGI	Post-TGI
Intracranial pressure (mmHg)	19.3±5.8	18.8±5.2	17.4±4.3
Cerebral perfusion pressure (mmHg)	76.3±10.9	78.8±10.8	74.1±9.5
Jugular venous oxygen saturation (%)	72±9	73±9	71±10
Right cerebral middle artery mean velocity (cm/s)	73±67	77±62	74±63
Right cerebral middle artery pulsatility index	1.3±0.5	1.1±0.5*	1.1±0.3
Left cerebral middle artery mean velocity (cm/s)	63±48	77±58*	73±54
Left cerebral middle artery pulsatility index	1.3±0.3	1.2±0.4	1.1±0.3

*$p \leq 0.05$ vs. basal
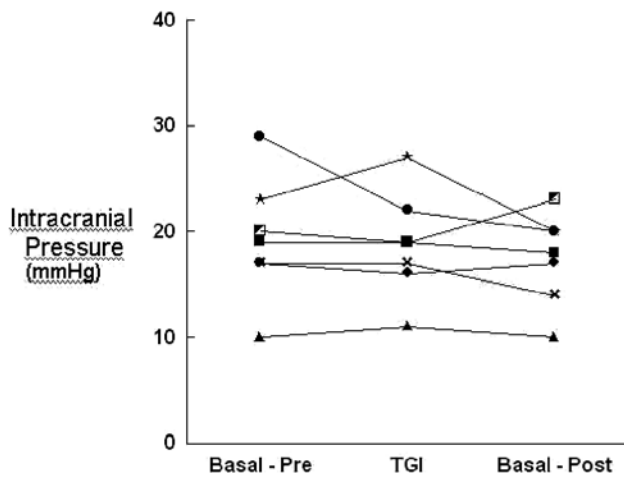
Fig. 3 Individual intracranial pressure values before, during, and after application of tracheal gas insufflation. Two patients showed a slight increase in intracranial pressure during tracheal gas insufflation application, but this was less than 20% of the increase that was previously defined as a reason to stop the study

high alveolar pressures. Clinical trials have demonstrated that the use of low V_T and airway plateau pressure are beneficial in terms of mortality and rate of weaning from mechanical ventilation [11, 12]. In our patients we applied TGI in an attempt to decrease the forces acting on the lungs, i.e., to convert a traditional ventilatory strategy into a protective one.

Physiological effects of TGI

This is the first study reported in the literature with an experimental design demonstrating the efficacy of TGI on CO_2 elimination in patients with head trauma. Tidal volume was reduced while $PaCO_2$ was maintained constant, showing that TGI is an effective technique to eliminate CO_2 in this setting. Expiratory TGI decreases $PaCO_2$ by diluting the CO_2 stored in the anatomical dead space proximal to the catheter tip, and, consequently, less CO_2 is reconveyed to the alveoli during the next inspiration. Secondly, a distal effect due to a superimposed jet generated at the catheter tip allows further removal of CO_2-laden gas from the distal portion of the tracheo-

bronchial tree [24, 25]. TGI is more effective in decreasing $PaCO_2$ in hypercapnic states due to high dead-space to V_T ratios [26], but TGI efficiency was maintained in our non-hypercapnic patients, who probably had a moderate amount of alveolar dead space and a considerable amount of instrumental/anatomical dead space. These results agree with those observed by Nakos et al. [14], who found that TGI may allow inspiratory tidal volume to be decreased while maintaining $PaCO_2$ constant even in patients with normal $PaCO_2$.

Successful application of TGI is limited by the potential for overpressurization of the airways and production of dynamic hyperinflation [27]. The development of autoPEEP with TGI is basically due to two factors: the reduction in the cross-sectional area of the tracheal tube and the effect of gas flow from the catheter directly toward the airways, both of which increase expiratory flow resistance [28]. It is likely that both factors were responsible for the increase in total PEEP detected in our patients during TGI. In our study an autoPEEP effect ensured that plateau pressure was not affected; consequently, our patients were ventilated with lower driving pressures and higher total PEEP during TGI, resulting in better oxygenation. Accordingly, we achieved a more protective strategy that decreased lung stretching while reducing lung derecruitment [11]. Potential concerns of expiratory TGI at moderate/high flows include bronchial mucosal damage as well as inspissation or retention of secretions, especially if the insufflated gas is not humidified for prolonged periods. The presence of a catheter inside the endotracheal tube may complicate suction of respiratory secretions and sputum removal. It is possible to heating and humidify insufflated gas, but the high pressures that develop when the gas is forced through small-bore catheters may exceed the humidifier's leak or burst pressure [29, 30]. Therefore further investigations on the above safety concerns are warranted for routine use of expiratory TGI for long term periods.

We used phasic mid- to end-expiratory TGI because it is as effective as continuous TGI to improve CO_2 clearance [31]. Expiratory TGI during volume control ventilation prevents the delivery of additional V_T because gas flow stops at the end of expiration, while continuous TGI needs a reduction in V_T proportional to the amount of gas delivered by TGI during inspiration. Additionally, we

used low TGI flow and we placed the catheter tip 2 cm above the carina to minimize the risk of impaired ventilatory efficiency and airway trauma [13, 32].

Effects of TGI on cerebral parameters

We observed no significant changes in ICP, CPP, jugular venous oxyhemoglobin saturation, or transcranial Doppler before, during, or after TGI except for a slight decrease in the pulsatility index of the right middle cerebral artery and an increase in the mean velocity of the left middle cerebral artery, but both were in the physiological range without clinical significance. One of the key aspects of these results is that we maintained normocapnia throughout the study by continuous monitoring of blood gases, allowing a progressive reduction in V_T, thus ensuring a constant value of $PaCO_2$. Additionally, the observed stability in mean arterial pressure and ICP during the study ensured the same levels of CPP. Recently Bein et al. [33] tested the effect of lung recruitment maneuvers in patients with head injury and found that cerebral hemodynamics deteriorated with this technique because mean arterial pressure reduction led to impaired ICP and CPP.

Patients with head trauma are usually ventilated with low levels of PEEP to avoid deleterious elevations in intrathoracic pressure, which can impair cerebral venous outflow and intracranial pressure regulation [5]. Nevertheless the effects of PEEP on intracranial pressure and cerebral perfusion pressure are still under debate [34, 35, 36]. The increase in total PEEP observed with TGI did not alter any cerebral parameters in our patients. PEEP may improve oxygenation and reduce the toxicity of high levels of FIO_2, but it could be deleterious by increasing intrathoracic pressure, with associated reduction in cardiac output, and thereby bring about a reduction in CPP.

In our patients PEEP was well tolerated for several possible reasons. First, the average increase in total PEEP was moderate (<5 cmH$_2$O). Second, our patients had decreased compliance of the respiratory system, and presumably a smaller portion of PEEP was transmitted to the intrathoracic blood vessels and to the intracranial compartment in this setting [37]. Third, our patients were in the supine position with a head elevation close to 30° and with the neck completely aligned. Fourth, the basal value of ICP in our patients was 19.3 mmHg, a value higher than total PEEP [35, 36]. The vascular waterfall theory [38] postulates that ICP acts as the effective upstream pressure. Therefore a PEEP-related increase in intrathoracic pressure higher than basal ICP would be needed to impair cerebral venous outflow. In agreement with this theory, it was unnecessary to stop our study due to impairment in any of the cerebral parameters.

Our data suggest that TGI application is safe in patients with severe head trauma and ALI/ARDS, and that it allows them to be ventilated with a more protective ventilatory strategy. However, the small sample size in this study does not allow extrapolation to wide populations of patients with acute brain injury. Conceivably TGI could be a useful adjunct to mechanical ventilation in head trauma patients and may decrease the lung contribution to the inflammatory response that can affect distal organs [39] and even the brain.

Conclusions

In patients with severe head trauma and acute lung injury the application of phasic TGI (at mid- to end-expiration) allows ventilation with lower V_T and driving pressure while maintaining $PaCO_2$ constant without any deleterious effects on the cerebral parameters.

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