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Inappropriate Prehospital Ventilation in Severe Traumatic Brain Injury Increases In-Hospital Mortality

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Abstract

In the setting of acute brainstem herniation in traumatic brain injury (TBI), the use of hyperventilation to reduce intracranial pressure may be life-saving. However, undue use of hyperventilation is thought to increase the incidence of secondary brain injury through direct reduction of cerebral blood flow. This is a retrospective review determining the effect of prehospital hyperventilation on in-hospital mortality following severe TBI. All trauma patients admitted directly to a single level 1 trauma center from January 2000 to January 2007 with an initial Glasgow Coma Scale (GCS) score ≤ 8 were included in the study ($n = 77$). Patients without documented or with late (>20 min) arterial blood gas at presentation ($n = 12$) were excluded from the study. The remaining population ($n = 65$) was sorted into three groups based on the initial partial pressure of carbon dioxide: hypocarbic ($Pco_2 < 35$ mm Hg), normocarbic (Pco_2 35–45 mm Hg), and hypercarbic ($Pco_2 > 45$ mm Hg). Outcome was based on mortality during hospital admission. Survival was found to be related to admission Pco_2 in head trauma patients requiring intubation ($p = 0.045$). Patients with normocarbia on presenting arterial blood gas testing had in-hospital mortality of 15%, significantly improved over patients presenting with hypocarbia (in-hospital mortality 77%) or hypercarbia (in-hospital mortality 61%). Although there are many reports of the negative impact of prophylactic hyperventilation following severe TBI, this modality is frequently utilized in the prehospital setting. Our results suggest that abnormal Pco_2 on presentation after severe head trauma is correlated with increased in-hospital mortality. We advocate normoventilation in the prehospital setting.

Key words: brain injury guidelines; hyperventilation; prehospital; traumatic brain injury

Introduction

It is generally accepted that the goal of management following severe traumatic brain injury (TBI) is to prevent secondary brain injury (Chestnut et al., 2002; The Brain Trauma Foundation, 2007). The virtues of hyperventilation in controlling intracranial pressure (ICP) to this end were first described nearly 50 years ago (Lassen, 1966; Lundberg et al., 1959), although no study to date has clearly defined this intervention as reducing morbidity or mortality in severe TBI. Conversely, the largest prospective study of hyperventilation revealed that prolonged hyperventilation had an adverse effect (Muizelaar et al., 1991).

The effect of hyperventilation to reduce ICP is well understood. Hyperventilation causes cerebral vasoconstriction through the potent vasomotor effect of hypocarbia, thus decreasing ICP by reduced cerebral blood volume (Chestnut et al., 2002; Raichle and Plum, 1972). Experimentally this effect is evident; the potent vasomotor effects of carbon dioxide induce a 3% decrease in cerebral blood flow (CBF) for every 1 mm Hg drop in Pco_2 within the physiologic range (Deem, 2006; Kety and Schmidt, 1948; Raichle and Plum, 1972; Stochetti et al., 2005). This principle has been applied for many years in neuroanesthesia to improve operative conditions (Lundberg et al., 1959). Scattered reports of improved outcome from head trauma with hyperventilation solidified its use in traumatic head injury for many years as the standard of care (Crockard et al., 1973; Gordon, 1971; Rossandra et al., 1972). Additionally, it has been proposed that hyperventilation may reduce the incidence of secondary injury by decreasing intracranial pH, thereby reducing the lactic acidosis associated with TBI (Lassen, 1966; Muizelaar et al., 1991).

With clear theoretical benefits but little clinical proof of efficacy, the Brain Trauma Foundation (BTF) has published guidelines for the use of hyperventilation in trauma (The Brain Trauma Foundation, 2000b, 2007). The basis of these guidelines is the overwhelming evidence of the detrimental effects of hyperventilation in the setting of severe TBI with

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regard to increasing secondary brain injury by decreasing CBF, but sporadic success of ICP reduction in the face of acute herniation.

Experimental studies of cerebral blood flow following severe TBI have elucidated the mechanism by which hyperventilation may be detrimental shortly following trauma. Many authors have confirmed decreased global CBF in the first day after TBI (Bouma et al., 1991; Coles et al., 2004; Marion et al., 1991; Overgaard and Tweed, 1974). This is particularly true in patients with diffuse cerebral edema, and has been characterized as well in patients with traumatic mass lesions (Bouma et al., 1991; Schmidt et al., 2003). This drop in CBF normalizes and typically develops into a relatively hyperemic state, with cerebral blood flow exceeding metabolic demand in the 24- to 48-h window post-injury (Martin et al., 1997). Data extrapolated from these studies suggest that the decrease in CBF following TBI is of greatest significance immediately following the injury (Bouma et al., 1991; Marion et al., 1991). This is supported by animal models, that show a decrease in CBF (Pfenninger et al., 1989) and CPP (Zauner et al., 2002) within minutes following fluid percussion injury.

When hyperventilation is superimposed on this phenomenon, a relative ischemia ensues, resulting in tissue acidosis tantamount to secondary brain injury. This theory is strengthened by studies showing that following trauma metabolites such as lactic acid are found in higher concentrations, and that these higher concentrations are seen following even very short periods of hyperventilation (Marion et al., 2002). On autopsy, the effect of ischemic changes on brain tissue have been confirmed in most patients with fatal severe TBI (Graham and Adams, 1971).

If the concept of relative ischemia in the early post-injury period is accepted, very early (i.e., prehospital) intervention to prevent secondary injury should be a goal in the management of TBI. This role will fall into the hands of first responders and transport teams en route to the trauma center. As noted in the literature, the tendency of prehospital ventilation of patients with TBI is toward hyperventilation, whether indicated or not by the BTF guidelines (Helm et al., 2003; Lal et al., 2003). We anecdotally noted at our center that patients with TBI tended to be indiscriminately hyperventilated regardless of the presence or absence of signs of brainstem herniation. This observation is not unique to our hospital and has been commented on previously (Di Bartolomeo et al., 2003; Thomas et al., 2002). This observation prompted our study, the primary goal of which was to determine if inappropriate hyperventilation in head-injured patients was contributing to mortality of brain-injured patients, presumably through secondary brain injury.

Methods

This study is a retrospective chart review. Data were extracted from our institutional trauma database collected from chart review by non-physician members of the trauma team. At our institution the trauma database was reformed as of January 2000, thus no data prior to this date were used. Study subjects included all patients age >17 years presenting directly to Fletcher Allen Health Care (FAHC) from site of injury between the dates of January 2000 and January 2007 with initial Glasgow Coma Scale (GCS) scores <8 ($n = 77$). This eliminates a significant portion of our trauma population, those patients presenting to non-tertiary care centers, who are typically transferred to our facility following primary survey. Patients with no documented presenting arterial blood gas or blood gas acquired more than 20 min after arrival ($n = 12$) were excluded from this study. The remaining population ($n = 65$) was sorted based on initial partial pressure of carbon dioxide (Pco_2) into three groups: hypocarbic/hyperventilated ($Pco_2 < 35$ mm Hg), normocarbic (Pco_2 35–45 mm Hg), and hypercarbic/hypoventilated ($Pco_2 > 45$ mm Hg), based on the normal levels accepted by our institution.

Patients are not intubated by first responders or during transport at our hospital, thus no patients in this group were intubated prior to arrival at the hospital. Patients receive manual bag-mask breaths throughout transport to the trauma center. Routine trauma protocol is for arterial blood gas to be acquired concurrently with commencement of primary survey. Our standard of data collection is for arterial blood gas to be acquired as rapidly as possible, with using portable point-of care analyzers. Point-of-care analyzers allow alterations in physiological state such as hypothermia, and provide results within minutes. Due to the technical detail of acquisition of arterial blood gases, no standards of time of intubation or initiation of mechanically delivered ventilation exist. All blood gas levels acquired 20 min or more following arrival in the hospital were eliminated from the study.

Variables thought to be potential confounders, including age, sex, level of arousal (GCS; Teasdale and Jennett, 1974), Injury Severity Score (ISS; Baker et al., 1974), evidence of brainstem herniation or mass lesion by examination, partial pressure of oxygen, transit or intra-resuscitative hypoxia and apnea, and time of transit, were either extracted from the original record or the database as available. With few exceptions, an intracranial pressure (ICP) monitor or ventriculostomy were placed in this population shortly following admission. Craniotomy performed during admission was recorded. Primary outcome was in-hospital mortality.

The GCS score was that recorded on arrival by the appropriate member of the trauma team, typically the on-call neurosurgery resident. ISS was defined as initially described (Baker et al., 1974), and was included as a measure of multisystem trauma. Brainstem herniation was defined as localizing findings on initial examination. Hypoxia was defined as $Pao_2 < 60$ mm Hg, or definitive cyanosis or apnea reported by the transport team or during resuscitation. Hypotension was defined as systolic blood pressure <90 mm Hg, or pulselessness recorded by the transport team or during resuscitation. Time of transit was time of arrival at FAHC less time of call to scene as recorded by the paramedic team, and was incompletely recorded for all patients.

The independence of analog data variables considered to be potentially confounding, and primary outcome of in-hospital mortality, was analyzed with a 3×2 Fischer's exact test. The independence of normal variables was analyzed with analysis of variance (ANOVA). For both Fischer's exact test and ANOVA analysis, the 5% level was used to define statistical significance. Data were compared with online statistics calculation software (http://faculty.vassar.edu/lowry/VassarStats.html).

Statistical analysis

For multivariate analysis, continuous and nominal data were dichotomized and binary logistic regression performed

Table 1. Study Group Characteristics

Pco_2 (mm Hg)	<35	35–45	>45	p
No.	17	20	28	
Age (y)	54.1*	35.6	37.0	0.003
Percentage of males (%)	71	70	75	1.000
GCS score (average)	4.6	6.0	4.8	0.071
ISS (average)	29.6	27.9	33.0	0.415
Abnormal pupillary exam (%)	47	25	50	0.515
Evidence of brainstem herniation by exam (%)	18	25	36	0.622
Po_2 (mm Hg, average)	242	285	245	0.700
Hypoxia and hypotension during resuscitation (%)	35	5	25	0.170
Transport time (min)	36.0	40.9	40.9	0.583
Craniotomy performed during hospitalization (%)	24	25	32	0.889
In-hospital mortality (%)	77*	15*	61*	0.045

*Statistically significant to $p < 0.05$ between groups.
Pco_2, partial pressure of carbon dioxide; Po_2, partial pressure of oxygen; ISS, Injury Severity Score; GCS, Glasgow Coma Scale.

using SPSS software (SPSS 16.0 for Windows). Data were dichotomized as follows: Pco_2 normal (between and including 35 and 45 mm Hg) or abnormal (all other values); age greater than 50 or less than 50 years; GCS scores 3–5 or 6–8; and ISS scores greater than and including 25 or less than 25. All variables found to be independent predictors of death by independent analysis to a level of significance of 5% were included in the multivariate logistic regression.

Results

In-hospital mortality

Sixty-five patients were included in the study group. The mechanism of injury was most commonly motor vehicle collisions (32/65, 49%). The remaining half of injuries were acquired via fall (20), gunshot wound (5), skiing (3), or other (8). The inequity of penetrating to blunt trauma is characteristic for our center. The most frequent injury diagnosed was subdural hematoma (17/65, 26%). The remaining list of injuries includes subarachnoid hemorrhage (8), contusion/concussion (7), diffuse axonal injury (6), diffuse edema/hypoxia (6), epidural hematoma (5), ballistic/penetrating (5), fracture (5), intraparenchymal hematoma (4), and undiagnosed (2).

The characteristics of the study group are outlined in Table 1. The groups are statistically matched in all groups with the exception of age ($p = 0.003$). The hypocarbic group had a significantly older population (mean age 54.1 years) compared with the other groups (mean age 36.4 years). The normocarbic and hypercarbic groups were matched for age ($p = 0.787$).

Our data display a correlation between presenting Pco_2 and in-hospital mortality (Fig. 1). The overall death rate for our population was 51%. The in-hospital mortality in patients with hypocarbia (13/17; 76.5%), normocarbia (3/20; 15.0%), and hypercarbia (17/28; 60.7%) were highly variant ($p = 0.045$). The death rate for patients with abnormal Pco_2 values on presentation had considerably worse in-hospital mortality, whereas normocapnea on presenting arterial blood gas was correlated with significantly decreased in-hospital mortality.

For non-survivors, the cause of death was from head injury for nearly all (26 of 33, 79%) patients. The most frequent cause of death was brain death (12/33, 36%) or withdrawal (14/33, 42%) of care by family request due to severity of coma in the absence of brain death. Seven patients had non-neurological causes listed as the primary cause of death. Of these patients, four had asystole (3 on the day of trauma, 1 on hospital day 14), two died of hemorrhagic shock, and one had sepsis from colitis before care was withdrawn on the 26th day after trauma.

Inappropriate use of hyperventilation

In our study group, a majority of patients 46 of 65 (72%) had no evidence of brainstem herniation on initial CT scan. Only 3 of 17 (18%) hypocarbic (hyperventilated) patients had evidence of brainstem herniation, while ironically 25% of normocarbic (normoventilated) and 36% of hypercarbic (hypoventilated) patients had evidence of brainstem herniation.

Overall, only 3 of 19 (16%) patients with evidence of brainstem herniation were hyperventilated, while 14 of 46 (30%) severely head-injured patients with no evidence of

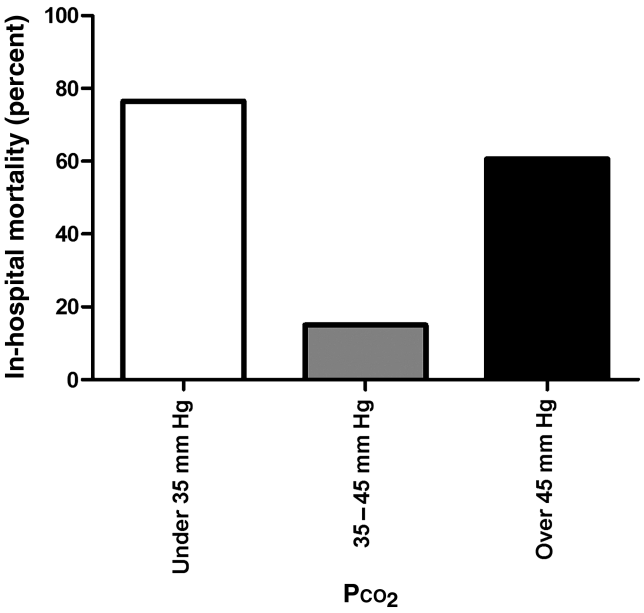

FIG. 1. Partial pressure of carbon dioxide (Pco_2) as an independent predictor of mortality in traumatic brain injury.

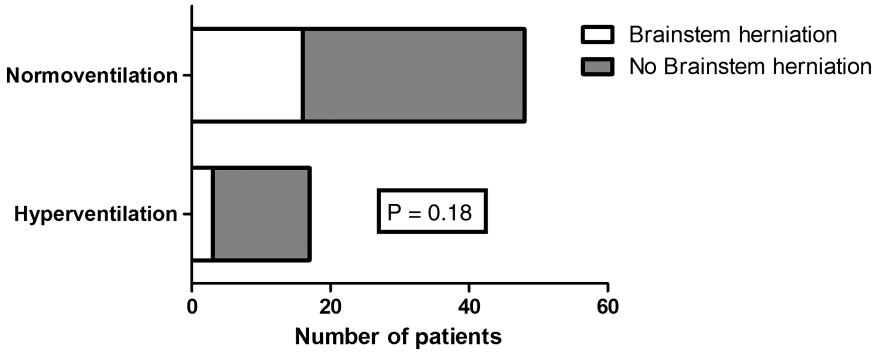

FIG. 2. Hyperventilation, normoventilation, and brainstem herniation.

brainstem herniation were improperly hypocarbic (hyperventilated). Nearly half of patients (30/65, 46%) were not treated in accordance with the recommendations of the BTF. For example, 15 patients with signs of brainstem herniation were not hyperventilated. These results are summarized in Fig. 2.

Multivariate analysis

Because of the potential confounding factors delineated above, a multivariate analysis was performed for predictors of in-hospital mortality. Recorded variables found to be independent risk factors for in-hospital mortality were included in this analysis (Tables 2 and 3). For this cohort of patients, the most significant risk factors for prediction of death included age older than 50 years and abnormal $Paco_2$ on presentation (Table 4). Surprisingly, classical measures of severity of coma and injury (GCS and ISS) did not factor as strongly into prediction of death as one might expect (Table 3). This is likely explained by selection bias, as all patients in the cohort had relatively severe TBI with coma.

Discussion

Measurement of the partial pressure of carbon dioxide and ventilatory status

Ventilatory status following brain injury has been well studied (Vicario et al., 1983). It is not surprising that there is a direct correlation between low level of arousal and a decrease in ventilatory drive and hypercarbia. A patient suffering severe brain injury may have patterns of both spontaneous hyperventilation and hypoventilation, though there is a tendency toward hypoventilation and hypercarbia in those with the lowest scores on the Glasgow Coma Scale (Vicario et al., 1983). Because of the irregular breathing patterns and frequent hypoventilation encountered with severe TBI, early intervention with control of airway and manual or mechanized ventilation is recommended for optimal outcome (Davis et al., 2005).

Table 2. Univariate (Chi-Square) Analysis

Variable	*Chi-square*	p
Pco_2	14.7	<0.001
Age	17.4	<0.001
Male gender	1.41	0.236
GCS score	6.78	0.009
ISS	5.64	0.018
Brainstem herniation	5.64	0.018
Hypoxia and hypotension	11.2	0.001
Surgery	0.228	0.633

ISS, Injury Severity Score; GCS, Glasgow Coma Scale; Pco_2, partial pressure of carbon dioxide.

At our institution, prehospital trauma care is implemented by trained emergency technicians and volunteers, but few trained paramedics. As a result, patients arriving directly to the hospital from the site of injury are not intubated, but instead mechanical breaths are delivered manually via bag-mask throughout transport, if needed.

Throughout this article, the terms hypocarbia/hyperventilation and hypercarbia/hypoventilation are used in an interchangeable manner. It is important to recognize the limitations of using Pco_2 as a surrogate of ventilation status. Significant changes in partial pressures of blood gases can be seen only a few minutes after changes in ventilatory parameters (Marion et al., 2002). Several patients had over 60 min of transport time, and it is clearly simplistic to suppose that a single arterial blood gas measurement can accurately represent a full hour of manually-delivered breaths. In this retrospective analysis of patients with TBI not on mechanical ventilators, this may be particularly evident. However, even short runs of hyperventilation have been shown to have effects on cerebral blood flow dynamics (Marion et al., 2002), and these inappropriate ventilatory parameters, no matter the duration, seem to have an effect on mortality in patients with TBI. Additionally, other authors have described a similar correlation between the initially measured partial pressure of carbon dioxide and outcome of TBI (Davis et al., 2006).

A superior study would involve patients suffering TBI randomized into equal groups of hyperventilated, normoventilated, and hypoventilated groups, with in-transit monitoring of Pco_2. Such a study would require great coordination and training that would not be possible in our current primary response system. We acknowledge that the small sample size represented here, as well as our unique prehospital treatment system, may limit the applicability of our results to larger treatment facilities.

Inappropriate prehospital ventilation increases in-hospital mortality from traumatic brain injury

The primary outcome of in-hospital mortality had significant variance between the three groups (Fig. 1). This effect

Table 3. Binary Multivariate Regression Analysis Summary

Variable	*Coefficient (B)*	*Standard error*	*Wald*	p	*Odds ratio*	*95% CI*
Intercept	−4.84	1.43	11.5	0.001	—	—
Pco_2 (<35 or >45 mm Hg)	2.65	1.03	6.65	0.010	14.2	1.89,106
Age (>50 years)	2.57	0.850	9.16	0.002	13.1	2.48,69.3
GCS (<6)	0.623	0.842	0.548	0.0459	1.87	0.358,9.71
ISS (>25)	1.00	1.01	0.974	0.324	2.72	0.373,19.8
Brainstem herniation	1.78	0.980	3.29	0.070	5.92	0.867,40.3
Hypoxia and hypotension	1.30	1.23	1.12	0.290	3.66	0.331,40.5

ISS, Injury Severity Score; GCS, Glasgow Coma Scale; Pco_2, partial pressure of carbon dioxide; CI, confidence interval.

appears to be independent of other variables known to be correlated with poor outcome from TBI. We propose that these differences are accounted for by the complex physiological changes induced by alterations in the partial pressure of carbon dioxide. These physiologic responses promote suboptimal conditions following TBI, which induces secondary brain injury and associated clinical morbidity. This presents a potential therapeutic strategy for the prevention of secondary brain injury in TBI, via normalization of Pco_2.

The hypocarbic group had the greatest in-hospital mortality rate. The presumed physiologic response to Pco_2 causing this difference is vasoconstriction induced by hypocarbia, in concert with the physiologic decrease in CBF known to exist after TBI (Bouma et al., 1992; Marion et al., 1991). This drop in CBF, which diminishes blood flow and brain oxygenation, causes overwhelming ischemia despite relatively diminished metabolic needs (Deem, 2006), resulting in secondary brain injury and higher mortality. This model suggests that in the first 1–2 h following trauma, the CO_2 vasoreactivity of cerebral blood vessels is undisturbed (Diringer et al., 2002; Marion et al., 2002); however, this is not universally noted in patients with severe traumatic head injury (Lassen, 1966). The disproportionate mortality in this group may be correlated with inappropriate use of hyperventilation in absence of elevated ICP. In such circumstances, there is no indication for hyperventilation therapy (The Brain Trauma Foundation, 2000b). Such patients comprised a majority of this group (14/17, 82%).

The hypercarbic group had higher mortality than average. To some degree this was surprising, as we have seen improvement in physiological parameters with permissive hypercarbia/hypoventilation in a fluid percussion model of TBI in swine (unpublished data), and other authors have suggested hypoventilation as a potential therapeutic strategy (Manley et al., 2000). In a normal physiological setting, hypercarbia/hypoventilation induces an increase in CBF by a reverse mechanism of hypocarbia/hyperventilation (Deem, 2006; Stochetti et al., 2005). In concert with the known decrease in CBF following TBI, this vasodilating response to hypercarbia would normalize CBF. As an additional benefit, the oxygen-hemoglobin dissociation curve would be right-shifted due to the change in Pco_2, allowing for improved $P_{br}O_2$ (Deem, 2006; Hemphill et al., 2001; Stochetti et al., 2005). However, this effect has not been reliably reproduced in animal models (Anderson et al., 1988; Manley et al., 1999), and no evidence of benefit from hypercarbia was seen in our study group. The explanation of this is likely due to an alteration of the normal physiology of the system induced by TBI, but the exact mechanism of change is unclear. The CO_2 reactivity of cerebral vessels appears to be diminished but preserved following TBI (Diringer et al., 2002;, Marion et al., 2002), although the relationship of $P_{br}O_2$ to Pco_2 does not (Diringer et al., 2002; Imberti et al., 2002; Van Santbrink et al., 1996). Neither of these parameters are well studied in clinical studies in the acute period (<2 h) following TBI. Perhaps in the acute setting following brain injury, suboptimal CO_2 vasoreactivity causes a left shift of the CBF-Pco_2 curve (Fig. 3), with preserved CO_2 reactivity to hyperventilation, but buffered vasodilation to hypoventilation. This would cause a relative ischemia in both hypocarbic and hypercarbic groups, as well as increased mortality. Alternatively, the increase in CBF may have disturbed a delicate balance of ICP, raising it above a critical threshold, and thereby inducing secondary brain injury and increased morbidity. This may be the explanation for our study group, as a disproportionate number of patients in

Table 4. Age-Adjusted In-Hospital Mortality

	Pco_2	*Total number in subgroup*	*In-hospital mortality within subgroup*	*Percent in-hospital mortality*	p
Age <50 years	<35 mm Hg	5	3	60	<0.003
	35–45 mm Hg	17	1	6	
	>45 mm Hg	23	12	52	
All	<35 mm Hg	17	13	77	0.045
	35–45 mm Hg	20	3	15	
	>45 mm Hg	28	17	61	
Age >50 years	<35 mm Hg	12	10	83	0.175
	35–45 mm Hg	4	2	50	
	>45 mm Hg	5	5	100	

Pco_2, partial pressure of carbon dioxide.

Table 5. GCS-Adjusted In-Hospital Mortality

	Pco_2	*Total number in subgroup*	*In-hospital mortality within subgroup*	*Percent in-hospital mortality*	p
GCS score 3–5	<35 mm Hg	11	10	91	<0.010
	35–45 mm Hg	6	1	17	
	>45 mm Hg	16	11	69	
All	<35 mm Hg	17	13	77	0.045
	35–45 mm Hg	20	3	15	
	>45 mm Hg	28	17	61	
GCS score 6–8	<35 mm Hg	6	3	50	0.088
	35–45 mm Hg	14	2	14	
	>45 mm Hg	12	6	50	

GCS, Glasgow Coma Scale; Pco_2, partial pressure of carbon dioxide.

the hypercarbic/hypoventilated group had evidence of brainstem herniation on examination, suggesting that hyperventilation therapy may have had therapeutic benefit.

Normocarbic patients had low mortality compared with the average. These patients presumably have optimized CBF following TBI, thus minimizing secondary brain injury. Using presenting Pco_2 as a surrogate for ventilatory status, we thus suggest that normoventilation is of clear import in the very early (first 2 h) management of patients with severe TBI. Prehospital management of ventilation may be optimized by maintaining a normal Pco_2 unless there is evidence of acute intracranial hypertension and physical exam findings consistent with brainstem herniation syndrome.

Subgroup analysis: Age

A potential confounding factor in this study is age, which is known to have prognostic value following TBI. Patients aged more than 50 years suffering TBI have been shown to have poor outcomes (The Brain Trauma Foundation, 2000c). There was a statistically significant increase in age in the hypocarbic group ($p = 0.003$). This difference may be explained by undiagnosed pulmonary disease in the hypocarbic group, which could change baseline Pco_2. In our analysis, we did not take into account the presence of pre-existing morbidities. These data were not included in the analysis, as in our experience, such past medical history is frequently unclear or unknown at the initial presentation of most trauma patients. All patients were treated as equals in this regard.

The inequity in age between the groups allows for subgroup analysis. The cohort of 65 patients was divided into two groups: patients aged 50 or less, and patients older than age 50. These two groupings were then subdivided into hypocarbic, normocarbic, and hypercarbic groups as previously defined, and in-hospital mortality was compared. The results are summarized in Table 4. This yields a strong association between normocarbia and diminished in-hospital mortality ($p < 0.003$) in the group aged 50 years or less. In-hospital mortality was very high for all patients aged 50 or more (17/21, 81%). In this group, the trend toward improved survival is seen with all patients and patients aged under 50 years (Fig. 4), though the difference was not statistically significant ($p = 0.175$) due to limited power. Overall, the results suggest a strong correlation between in-hospital mortality and Pco_2 on admission for patients under age 50 years following severe TBI, and confirm the poor prognosis seen for patients with TBI aged over 50 years.

Subgroup analysis: Glasgow Coma Scale score

While there was no significant differences ($p = 0.071$) between GCS scores between the study groups, there was a clear trend toward improved level of consciousness in the normocarbic group (average GCS 6.00) compared with all other

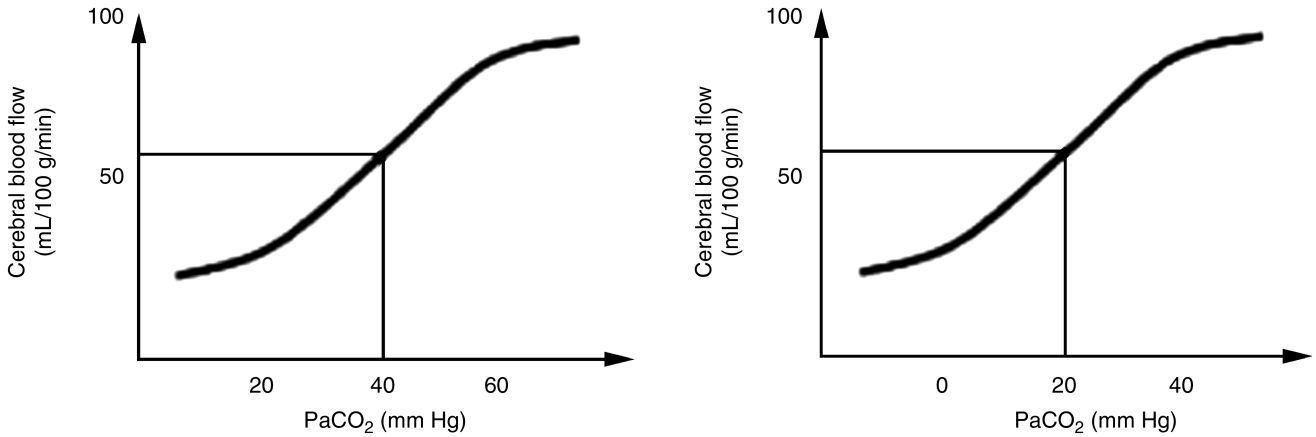

FIG. 3. Left shift of cerebral vasculature reactivity to carbon dioxide in traumatic brain injury (Pco_2, partial pressure of carbon dioxide).

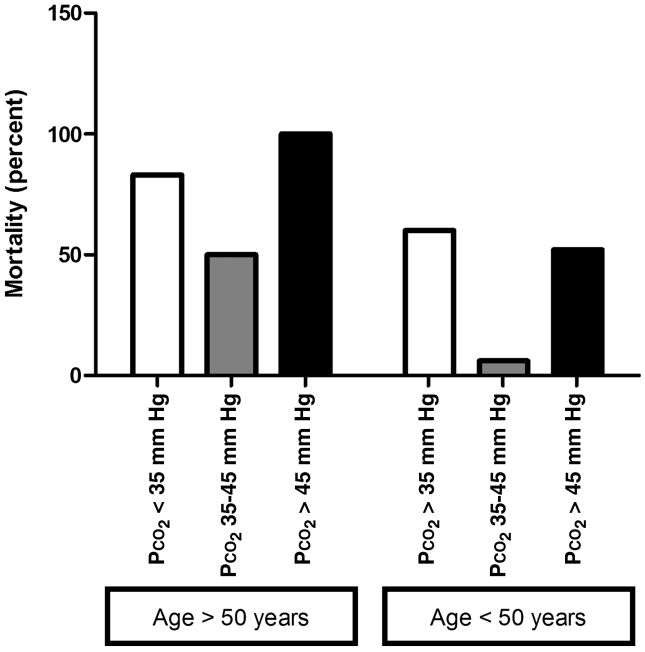

FIG. 4. Age-adjusted in-hospital mortality (Pco_2, partial pressure of carbon dioxide).

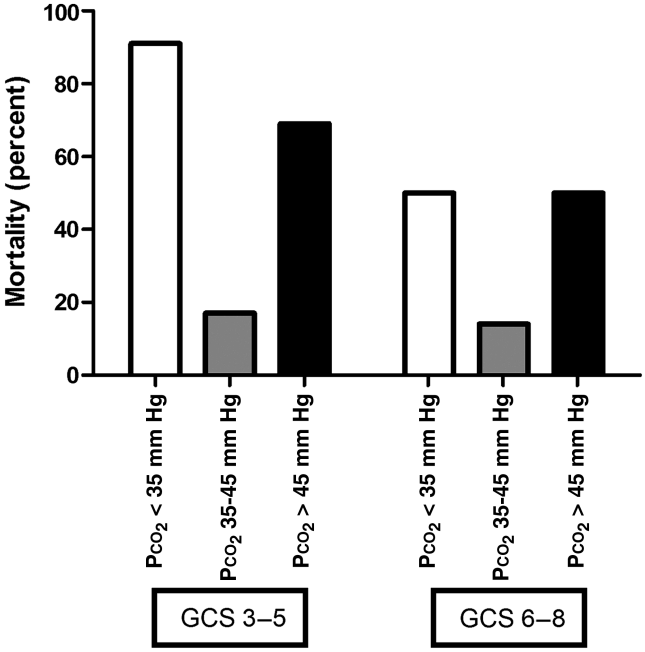

FIG. 5. GCS-adjusted in-hospital mortality (GCS, Glasgow Coma Scale score; Pco_2, partial pressure of carbon dioxide).

patients (GCS 4.76). As GCS is known to be an independent prognostic indicator of morbidity and mortality in TBI (The Brain Trauma Foundation, 2000a), subgroup analysis was performed to determine if this was a confounding factor.

The study population was divided into groups based on initial GCS score: those with GCS scores 3–5 and those with GCS scores 6–8. These two groupings were then subdivided into hypocarbic, normocarbic, and hypercarbic groups, as previously defined, and in-hospital mortality was compared. These results are summarized in Table 5. The results suggest a strong correlation ($p < 0.010$) between presenting Pco_2 and survival in patients with very low GCS scores, and statistically identical ($p = 0.088$) survival in the group with GCS scores of 6–8. Overall, the survival rates for patients with GCS scores of 6–8 (in-hospital mortality 34%) was improved over those with very low GCS scores on presentation (in-hospital mortality 67%), as would be expected. The subset analysis suggests that presenting GCS score may be a confounding factor in this analysis, although within the subgroups the overall trend toward improved outcomes is preserved (Fig. 5).

Avoidance of inappropriate hyperventilation in prehospital care of TBI patients

The BTF guidelines for prehospital ventilatory management recommend hyperventilation as an option for patients with signs of brainstem herniation upon examination (The Brain Trauma Foundation, 2000a, 2000b). There is no recommendation for prolonged hyperventilation, however. Using Pco_2 as a surrogate for ventilatory status, our study group was not treated in accordance with the BTF guidelines. Several patients (14/17, 82%) were hyperventilated (hypocarbic) on arrival, despite no evidence of brainstem herniation on examination. Conversely, many patients with evidence of brainstem herniation by examination were not hyperventilated (15/18, 83%). This provides an area for improvement in our prehospital care of patients with TBI.

Several authors have discussed the virtues of noninvasive surrogate measures of Pco_2, such as the end-tidal CO_2 monitor (Bhende and LaCovey, 2001; Deakin et al., 2004; Helm et al., 2003). This device allows an approximation of ventilatory status that may be easily applied to deliver proper ventilatory rates titrated to the desired values. There have been reports of improved results with this tool (Bhende and LaCovey, 2001), although additional study is needed before it is universally advocated for this population.

This study represents a small sample and may be limited in its global applicability due to the modern prehospital care present in most trauma systems. However, in this cohort there was a significant correlation between reduced mortality and normocarbia. The patients in our study group were transported an average of 41 min (range 9–136 min), and the results of this study indicate that there is an opportunity for improvement in patient care. We propose that a reasonable strategy for trauma centers such as ours is to aim for normocarbia using end-tidal CO_2 monitoring throughout transport from injury site to trauma center. At the trauma center, proper neurosurgical evaluation would determine whether hyperventilation is appropriate based on the Brain Trauma Foundation guidelines.

Conclusions

Our findings indicate: (1) hypocarbia/hyperventilation and hypercarbia/hypoventilation following TBI increases the risk of in-hospital mortality; and (2) normocarbia following TBI decreases the risk of in-hospital mortality.

We propose from these conclusions that abnormal physiologic states of hypercarbia and hypocarbia may induce secondary injury by inducing suboptimal oxygenation of brain

tissue during early (prehospital) management. Normocarbia appears to decrease the risk of mortality by maintaining a normal physiologic state and minimizing secondary brain injury.

We suggest that implementation of universal normoventilation of patients with TBI may be optimal prehospital management until an initial evaluation by neurosurgery personnel can be carried out. Alternatively, we advocate efforts to follow the guidelines of the BTF, and to initiate hyperventilation only with elevated intracranial pressure with signs of acute brainstem herniation on examination.

Author Disclosure Statement

No competing financial interests exist.

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