The Use of Quantitative End-Tidal Capnometry to Avoid Inadvertent Severe Hyperventilation in Patients With Head Injury After Paramedic Rapid Sequence Intubation

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Background: This study aimed to determine whether field end-tidal carbon dioxide CO_2 ($ETCO_2$) monitoring decreases inadvertent severe hyperventilation after paramedic rapid sequence intubation.

Methods: Data were collected prospectively as part of the San Diego Paramedic Rapid Sequence Intubation Trial, which enrolled adults with severe head injuries (Glasgow Coma Score, 3–8) that could not be intubated without neuromuscular blockade. After preoxygenation, the patients underwent rapid sequence intubation using midazolam and succinylcholine. A maximum of three intubation attempts were allowed before Combitube insertion was mandated. Tube confirmation was accomplished by physical examination, qualitative capnometry, pulse oximetry, and syringe aspiration. Standard ventilation parameters (tidal volume, 800 mL; 12 breaths/minute) were taught. One agency used portable $ETCO_2$ monitors, with ventilation modified to target $ETCO_2$ values of 30 to 35 mm Hg. Trial patients transported by aeromedical crews also underwent $ETCO_2$ monitoring. The primary outcome measure was the incidence of inadvertent severe hyperventilation, defined as arterial blood gas partial pressure of CO_2 (pCO_2) of less than 25 mm Hg at arrival, for patients with and those without $ETCO_2$ monitoring. These groups also were compared in terms of age, gender, clinical presentation, Abbreviated Injury Score, Injury Severity Score, arrival arterial blood gas data, and survival.

Results: The study enrolled 426 patients and administered neuromuscular blocking agents to 418 patients. Endotracheal intubation was successful for 355 of these patients (85.2%). Another 58 patients (13.6%) underwent Combitube insertion. For 291 successfully intubated patients, arrival pCO_2 values were documented, with continuous $ETCO_2$ monitoring performed for 144 of these patients (49.4%). Patients with $ETCO_2$ monitoring had a lower incidence of inadvertent severe hyperventilation than those without $ETCO_2$ monitoring (5.6% vs. 13.4%; odds ratio, 2.64; 95% confidence interval, 1.12–6.20; $p = 0.035$). There were no significant differences in terms of age, gender, clinical presentation, Abbreviated Injury Score, Injury Severity Score, arrival partial pressure of oxygen (pO_2) and pH, or survival. The patients in both groups with severe hyperventilation had a significantly higher mortality rate than the patients without hyperventilation (56 vs. 30%; odds ratio, 2.9; 95% confidence interval, 1.3–6.6; $p = 0.016$), which could not be explained solely on the basis of their injuries.

Conclusions: The use of $ETCO_2$ monitoring is associated with a decrease in inadvertent severe hyperventilation.

Key Words: Rapid sequence intubating, Paramedic, Traumatic brain injury, Capnometry, Hyperventilation.

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The ability of hyperventilation to lower omtracramoa; [ressire (ICP) via a decrease in cerebral blood volume is well documented. However, hyperventilation may lead to an even greater decrease in cerebral perfusion, resulting in ischemia.[1–9] Clinical evidence suggests that empiric hyperventilation worsens neurologic outcome, and current treatment guidelines recommend avoidance of hyperventilation except in cases of severe refractory intracranial hypertension or in the case of signs and symptoms that presage impending herniation.[10,11] Despite these recommendations, however, multiple studies have documented a high incidence of inadvertent hyperventilation in critically ill patients, especially in the prehospital environment.[1–3,12–21]

The San Diego Paramedic Rapid Sequence Intubation (RSI) Trial was designed to investigate the impact of paramedic-performed RSI on the outcome for patients with severe head injury. Whereas standardized ventilation parameters were used to target a partial pressure of carbon dioxide (pCO_2) value of 35 mm Hg, one agency instituted the use of quantitative end-tidal CO_2 ($ETCO_2$) monitors during the trial period to guide ventilation. This analysis investigates the impact of $ETCO_2$ monitoring on the incidence of inadvertent hyperventilation after paramedic RSI.

MATERIALS AND METHODS

Design

The San Diego Paramedic RSI Trial was a prospective, descriptive trial conducted over 3½ years from November 1998 to April 2002. This trial aimed to investigate the impact of paramedic RSI on outcome for patients with severe trau-

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matic brain injury. Data collected during the San Diego Paramedic RSI Trial were used for this analysis. Waiver of consent for the San Diego Paramedic RSI Trial was granted by the California State Emergency Medical Services (EMS) Board and by the investigational review board of each participating institution. Approval for this analysis was granted by the Human Subjects Program of the authors' institution.

Setting

There are 813 emergency medical treatment (EMT) paramedics accredited in San Diego County, which covers 4,261 square miles and contains 2.8 million people. In fiscal year 1996–1997, 12 different agencies performed 116,615 emergency transports. All but one agency participated in the trial. After completing home study material and a pretest, paramedics were trained in a 7-hour course, which included a video for teaching Glasgow Coma Scale (GCS) scoring, formal lectures on the pharmacology of RSI medications and the mechanics of performing this technique, multiple practice scenarios, and a posttest. The paramedics also received specific instruction as to optimal ventilation parameters, defined as 12 breaths per minute with an estimated tidal volume of 800 mL, and were allowed to practice with a stopwatch and spirometer.

Subjects

The target population for this study included adult major trauma patients with severe traumatic brain injury. The criteria for inclusion in the study required an apparent age of 18 years or older, major trauma victim status according to county protocols, transport time to the trauma center of 10 minutes or more, potential head injury by mechanism or physical examination, a Glasgow Coma Score (GCS) of 8 or less, and intubation impossibility without RSI. Subjects were excluded if intravenous access could not be established.

Therapeutic Intervention

All the subjects who met the inclusion criteria were preoxygenated via a non-rebreather face mask for 60 seconds. Bag valve mask ventilation was performed if pulse oximetry indicated an oxygen saturation (SaO_2) less than 95%. Patients were administered midazolam and succinylcholine using a simplified, weight-based dosing strategy. Midazolam was not given if systolic blood pressure was lower than 120 mm Hg. Paramedics were allowed three attempts at endotracheal intubation. If these were unsuccessful, Combitube (Kendall Company, Mansfield, MA) insertion was mandated. Tube placement was confirmed using physical examination findings, qualitative capnometry, pulse oximetry, and syringe aspiration. After confirmation of tube position, rocuronium was administered for continued paralysis during transport. Additional midazolam was administered after 30 minutes if systolic blood pressure remained at 120 mm Hg or higher, and morphine sulfate was administered in 2-mg increments for a "stress response," defined as a systolic blood pressure of 140 mm Hg or higher and a heart rate of 100 beats per minute or faster (Table 1).

Most paramedic agencies were given standardized ventilation parameters of 12 breaths per minute with a tidal volume of 800 mL, designed to achieve a pCO_2 value of 35 mm Hg. One agency instituted the use of handheld quantitative $ETCO_2$ devices (Tidal Wave; Novametrix Medical Systems, Wallingford, CT) during the second year of the trial. Paramedics with access to these devices were instructed to target an $ETCO_2$ recording of 30 to 35 mm Hg, and to avoid values of 25 mm Hg or lower. Many trial patients were ultimately transported by aeromedical crews, who also had access to $ETCO_2$ monitors (Propaq; Welch Allyn, Beaverton, OR) and were given identical ventilation guidelines. In the authors' prehospital system, the decision to transport a patient by helicopter is made by the ground paramedics. Distance from the receiving hospital and estimated transport time are the primary considerations in this decision.

Data Collection

Worksheets used during the RSI procedure provided detailed protocol instructions and served as data collection sheets. In addition, patient information was entered into an electronic database for San Diego County prehospital encounters and a county trauma registry for all major trauma victims. Finally, paramedics paged one of the principal investigators within 1 hour of the RSI procedure to answer additional questions regarding the procedure and to review GCS calculations. Collected data included patient demographics and mechanism of injury, initial clinical presentation including GCS score and vital signs, an Abbreviated Injury Score (AIS) for each body system and an Injury Severity Score (ISS), number of intubation attempts, initial and final SaO_2 values, arterial blood gas (ABG) values at the patient's arrival in the trauma center, and mortality.

Table 1 Rapid Sequence Intubation Medication Protocols Used During the Trial[a]

	Small	Average	Large
	80–140 lbs (35–63 kg)	141–225 lbs (63–100 kg)	>225 lbs (>100 kg)
Midazolam	2 mg	2.5 mg	3.0 mg
Succinylcholine	4 ml (80 mg)	6 ml (120 mg)	8 ml (160 mg)
Rocuronium	4 ml (40 mg)	6 ml (60 mg)	8 ml (80 mg)
Morphine	2 mg every 10 min for stress response (SBP > 140 mm Hg; HR > 100 bpm)		

SBP, systolic blood pressure; HR, heart rate; bpm, beats per minute.
[a] This simplified dosing strategy allowed for a constant volume of paralytic medication for patients in a given weight stratification.

Data Analysis

The primary outcome measure for this analysis was the incidence of severe inadvertent hyperventilation after paramedic RSI with the use of quantitative $ETCO_2$ monitoring, as compared with the use of standardized ventilation parameters. Hyperventilation was defined as an arrival pCO_2 value lower than 25 mm Hg. Patients transported by aeromedical crews were excluded from this analysis. Also excluded were patients unable to be intubated and those undergoing Combitube insertion. The number of patients in each group with pCO_2 values falling into the category of 5-mm Hg increments was displayed graphically. Comparisons between the two groups also were performed with regard to demographics, mechanism of injury, AIS for each body system, ISS, vital signs, field oxygen saturation (SaO_2) values, number of intubation attempts, ABG values, and serum ethanol. The overall mortality and incidence of death on the first hospital day also were recorded. To explore the potential impact of hyperventilation on outcome, secondary analysis involving all the patients compared the patients who had inadvertent severe hyperventilation (arrival pCO_2, <25 mm Hg) with those who had no severe hyperventilation in terms of all the aforementioned parameters. Flow diagrams for the primary and secondary outcome measures are displayed in Figure 1.

Statistical Analysis

Odds ratios (OR) with 95% confidence intervals (95% CI) were used to compare patients who had quantitative $ETCO_2$ monitoring with those subjected to standardized ventilation parameters in terms of the incidence of severe hyperventilation, as defined earlier. Student's *t*-testing, χ^2, and rank-sum testing were used when appropriate to compare the two groups with regard to the other aforementioned variables. Significance was assumed for *p* values less than 0.05. Statistical calculations were performed using Analyze-It (Analyze-It Software, Leeds, UK).

RESULTS

During the study period, 426 patients were identified as meeting the inclusion criteria defined earlier. Two of these patients were intubated before paramedic contact, but received midazolam and rocuronium for paralysis during transport. Three patients did not receive succinylcholine, and an-

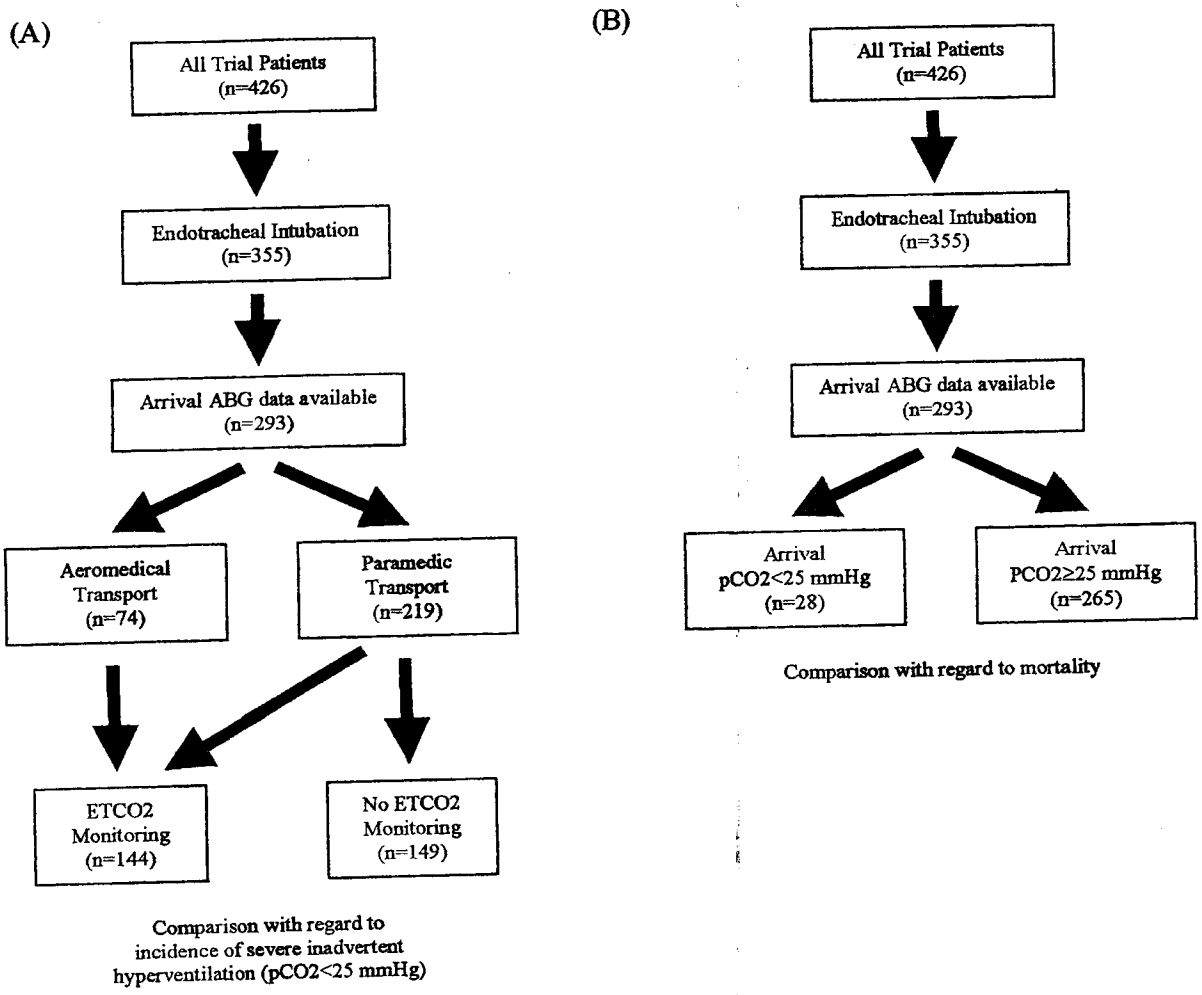


Fig. 1. *Study design flow diagram for primary (A) and secondary (B) outcome measures.*

other patient received one tenth of the protocol dose. None of these patients achieved appropriate relaxation for intubation. Of 420 patients, 355 (84.5%) were successfully intubated. Among the remaining 65 patients, 58 (89.2%) underwent successful Combitube insertion. As a result, 7 of the 420 patients (1.7%) arrived at the trauma resuscitation suite with an unsecured airway. There were no unrecognized esophageal intubations. Arrival pCO_2 values were available for 293 (82.5%) of the 355 successfully intubated patients. Of these patients, 144 (49.1%) had $ETCO_2$ monitoring during transport (70 patients with paramedics and 74 patients with aeromedical crews), and 149 (50.9%) were transported by paramedics without $ETCO_2$ monitoring.

Severe hyperventilation (arrival pCO_2, <25 mm Hg) was observed in 8 (5.6%) of 144 patients who had $ETCO_2$ monitoring, as compared with 20 (13.4%) of 149 patients who had no $ETCO_2$ monitoring (OR, 2.64; 95% CI, 1.12–6.20; $p = 0.035$). In the group of patients with $ETCO_2$ monitoring, severe hyperventilation was observed in 5 (7.1%) of 70 patients transported by paramedics and 3 (4.1%) of 74 patients transported by aeromedical crews. The mortality rates were similar between the two groups, including the incidence of death on the first hospital day. There were no significant differences between the groups in terms of demographics, mechanism of injury, clinical presentation, pre- and postintubation pulse oximetry values, arrival pO_2 or pH, and intubation success rates (Table 2). A histogram displaying the number of patients in each group with pCO_2 values falling into each interval group is displayed in Figure 2.

Secondary analysis showed higher mortality rates for patients with inadvertent severe hyperventilation (arrival pCO_2, <25 mm Hg) than for those without this condition (OR, 2.9; 95% CI, 1.3–6.6; $p = 0.016$). Patients with and those without inadvertent severe hyperventilation were similar in terms of demographic data, AIS, ISS, and vital signs (Table 3). The values for GCS and chest AIS both were lower in the group with severe hyperventilation, but these differences did not appear to be clinically significant. The notable exception was the incidence of gunshot wounds in the group with severe hyperventilation. However, this would have accounted for only three patients and does not completely explain the mortality difference. There was an expected decrease in pCO_2 and a corresponding increase in pH as well as a pO_2 increase for the severely hyperventilated patients.

Table 2 Demographic, Clinical, Intubation, and Arterial Blood Gas Data for Paramedic Rapid Sequence Intubation Patients Transported With and Without End-Tidal Carbon Dioxide ($ETCO_2$) Monitoring

Outcome Measure	Without ETCO2 Monitoring (n = 149)	With ETCO2 Monitoring (n = 144)	p Value
Demographics			
Age (years)	38.0	38.1	0.587
GCS score	4.9	4.9	0.692
Gender (% male)	81	78	0.760
Mechanism of injury			
Assault/struck by object	13	10	0.769
Bicycle accident	6	5	0.232
Fall	25	23	0.939
Found down	4	3	0.805
Gunshot wound	6	7	0.790
Motor vehicle accident	38	45	0.852
Pedestrian struck	9	10	0.142
Abbreviated Injury Scores			
Head/Neck	3.8	3.7	0.658
Face	0.5	0.6	0.397
Chest	1.1	1.3	0.326
Abdomen	0.8	0.7	0.308
Extremities	1.0	1.1	0.644
Skin	0.8	0.9	0.238
Injury Severity Score	25.7	26.8	0.537
Prehospital course			
Initial SBP (mm Hg)	122	125	0.784
Intubation attempts (n)	1.5	1.5	0.502
Preintubation SaO2 (%)	91.7	91.0	0.404
Postintubation SaO2 (%)	97.4	97.0	1.000
Transport time (min)	15.8	13.4	0.014[a]
Hospital data			
Arrival SBP (mm Hg)	137	142	0.737
Arrival HR (beats/min)	102	105	0.319
pH	7.36	7.35	0.489
pO2 (mm Hg)	331	311	0.317
pCO2 (mm Hg)	34.4	36.8	0.295
Base excess	−4.8	−4.2	0.289
Serum ethanol (mg/dL)	120	104	0.334
Overall mortality (%)	33	30	0.666
Death on hospital day 1 (%)	14	17	0.654

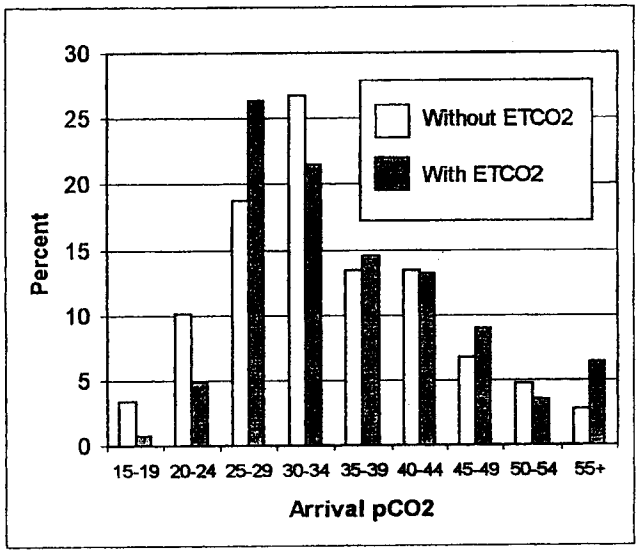
GCS, Glasgow Coma Score; SBP, systolic blood pressure; SaO_2, oxygen saturation; HR, heart rate; pO_2, partial pressure of oxygen; pCO_2, partial pressure of carbon dioxide.

[a] Significance is indicated for $p < 0.05$.

DISCUSSION

The technology for $ETCO_2$ monitoring has been available for many years in the intensive care unit and operating room. There has been reasonable correlation between $ETCO_2$ values and arterial pCO_2, especially for younger patients without pulmonary disease and in the absence of vigorous exercise.[22–28] Only recently has this technology been applied in the prehospital arena. Few attempts have been made to measure its accuracy or therapeutic value.[12,14,15] Thomas et al.[12] recently reported $ETCO_2$ values of 25 mm Hg or lower in one third of patients with severe head injuries transported by aeromedical crews. More than two thirds of these patients had at least one $ETCO_2$ value of 30 mm Hg or lower. Similar observations have been made for out-of-hospital patients, especially those with manual ventilation.[14,15] This report documents the efficacy of quantitative $ETCO_2$ monitoring in avoiding inadvertent severe hyperventilation in patients undergoing paramedic RSI.

Cerebral hemodynamics appear to play an important role for the patient with severe head injury. Intracranial hypertension can result in decreased cerebral perfusion pressure and global ischemia, whereas posttraumatic cerebral vasomotor



RSI = rapid sequence intubation

ETCO2 = end-tidal CO2

Fig. 2. *Frequency of various arrival partial pressure of carbon dioxide (pCO_2) intervals for paramedic rapid sequence intubation patients with and those without end-tidal carbon dioxide CO_2 ($ETCO_2$) monitoring during transport.*

dysfunction may result in regional hypoperfusion.[6–9,11] In addition, systemic hypotension from hemorrhage also decreases cerebral perfusion pressure and may exacerbate existing intracranial pathology. Cerebral autoregulatory mechanisms allow for therapeutic manipulation of cerebral blood volume and ICP through hyperventilation. Unfortunately, the decrease in cerebral blood volume and ICP with hyperventilation may come at the expense of cerebral perfusion, leading to concern for ischemia.[7,9,10] Multiple animal and human trials have demonstrated compromised oxygen delivery to cerebral tissue, with a decrease in pCO_2, and a multicenter, randomized, controlled trial has documented an increase in mortality with empiric use of hyperventilation for patients with severe head injury.[1–9,11,13–21] In addition, the authors' initial outcomes analysis documented an increase in mortality among hyperventilated patients.[29]

Another mechanism whereby hyperventilation may lead to worse outcomes for patients with head injury involves the effects of positive pressure ventilation on cardiac output. The decrease in intrathoracic pressure generated during inspiration for spontaneously breathing patients augments venous return, whereas positive pressure ventilation for the intubated patient obstructs venous return and can lead to a drop in cardiac output.[1,3,30,31] This effect is pronounced in the hypovolemic patient and may be especially detrimental for the patient with head injury, who is more susceptible to hemodynamic instability. Because hyperventilation involves a relative increase in inspiratory time, it has the potential to compromise cardiac output and further exacerbate posttraumatic cerebral ischemia. Current treatment guidelines recommend against the use of empiric hyperventilation for patients with severe traumatic brain injury.[10] Despite these recommendations, inadvertent hyperventilation appears to be relatively common in and out of the hospital environment, especially when manual ventilation is used.[12,14,15] Although it may be postulated that inadvertent hyperventilation would occur with greater frequency among more critically injured patients because of operator excitability, this study could not detect significant differences between the groups in terms of vital signs, GCS scores, AIS, ISS, overall mortality, or the incidence of death on the first hospital day.[1,12]

Table 3 Demographic, Clinical, Intubation, and Arterial Blood Gas Data for Patients With Inadvertent Severe Hyperventilation (pCO_2 < 25 mm Hg) and those without

Outcome Measure	Arrival pCO2 <25 mm Hg (n = 28)	Arrival pCO2 ≥25 mm Hg (n = 265)	*p* Value
Demographics			
Age (years)	38.4	38.0	0.926
GCS score	4.2	5.0	0.026[a]
Gender (% male)	75	80	0.706
Mechanism of injury			
Assault/struck by object	11	10	0.810
Bicycle accident	0	6	0.368
Fall	25	24	0.895
Found down	4	3	0.618
Gunshot wound	18	5	0.021*
Motor vehicle accident	32	42	0.427
Pedestrian struck	11	9	0.905
Abbreviated Injury Scores			
Head/neck	4.1	3.7	0.059
Face	0.4	0.5	0.633
Chest	0.4	1.3	0.038[a]
Abdomen	0.4	0.7	0.425
Extremities	0.7	1.0	0.395
Skin	0.9	0.9	0.817
Injury Severity Score	24.6	26.4	0.744
Prehospital course			
Initial SBP (mm Hg)	118	124	0.239
Intubation attempts (n)	1.4	1.5	0.688
Preintubation SaO2 (%)	93.0	91.2	0.858
Postintubation SaO2 (%)	98.6	97.1	0.263
Transport time (min)	15.2	14.9	0.744
Hospital data			
Arrival SBP (mm Hg)	137	140	0.885
Arrival HR (beats/min)	109	103	0.287
pH	7.45	7.35	<0.0001[a]
pO2 (mm Hg)	390	314	0.024[a]
pCO2 (mm Hg)	21.4	37.1	<0.0001[a]
Base excess	−5.6	−4.3	0.157
Serum ethanol (mg/dL)	97	115	0.680
Overall mortality (%)	56	30	0.016[a]
Death on hospital day 1 (%)	30	17	0.172

pCO_2, partial pressure of carbon dioxide; GCS, Glasgow Coma Score; SBP, systolic blood pressure; SaO_2, oxygen saturation; HR, heart rate; pO_2, partial pressure of oxygen.

[a] Significance is indicated for $p < 0.05$.

This study found that with the use of $ETCO_2$ monitoring, the incidence of severe inadvertent hyperventilation decreased from 13.4% to 5.6%. This suggests the efficacy of these devices in guiding prehospital ventilation, although $ETCO_2$ monitoring did not completely prevent the occurrence of severe hyperventilation. This may reflect the difficulty of performing multiple tasks in the back of a moving ambulance or the consequence of delays in obtaining an ABG, as discussed earlier. Secondary analysis showed an increase in mortality among patients with inadvertent severe hyperventilation that could not be explained on the basis of clinical parameters alone. It is unclear whether this represents an adverse effect of hyperventilation or an undetected difference in injury severity. Although the current analysis was not intended to explore the impact of hyperventilation on outcome, this mortality difference clearly warrants further investigation. Despite the association between hyperventilation and outcome, there was not a significant difference between the monitored and unmonitored groups in terms of overall mortality. This likely reflects the low overall incidence of severe hyperventilation in both groups. From these data, it can be estimated that inadvertent hyperventilation was prevented in 11 patients, and that slightly more than half of these (~6 patients) would have died. This study would have needed more than 10 ten times as many patients for these mortality differences to approach statistical significance.

One of the most significant limitations of this analysis involves the potential delays in obtaining ABG data at the patient's arrival in the trauma resuscitation suite. The standard of care in the authors' community requires an ABG to be drawn immediately for major trauma patients, especially when they arrive intubated. However, the exact time of arterial puncture relative to patient arrival and the ventilation parameters at that time were not available for analysis. Thus, it is possible that these pCO_2 values reflect ventilation parameters initiated by trauma center personnel rather than paramedics. In addition, there is no documentation as to whether $ETCO_2$ monitoring was available to guide ventilation in the resuscitation suite. Nevertheless, the significant decrease in the percentage of patients who had pCO_2 values less than 25 mm Hg with the use of $ETCO_2$ monitors suggests the efficacy of these devices in guiding prehospital ventilation.

No attempt was made to correlate the actual $ETCO_2$ reading with the ABG pCO_2 value at the patient's arrival. Although paramedics were asked to record arrival $ETCO_2$ values, these often were obtained while the patient was still inside the ambulance rather than at the time of delivery to the trauma suite, and thus were thought to be unreliable. These data also would likely suffer from reporting bias because of the specific ventilation protocols given to the paramedics. Finally, the patients undergoing Combitube intubation were excluded for the purposes of this analysis. The authors have previously documented the need for increased ventilation with the Combitube. They are of the opinion that it would be unfair to compare patients ventilated using standardized parameters designed for endotracheally intubated patients with patients undergoing $ETCO_2$-guided ventilation.[32] It is possible that $ETCO_2$ monitoring would be even more useful for Combitube-intubated patients because of its larger volume of dead space and the potential for air leakage around the two balloons.

CONCLUSIONS

The use of $ETCO_2$ monitoring to guide ventilation for patients with severe head injury undergoing paramedic RSI appears to prevent excessive hyperventilation. This was reflected by a decrease in the percentage of patients with arrival pCO_2 values of 25 mm Hg or lower, although the mean pCO_2 values were not significantly different between the patients undergoing $ETCO_2$ monitor-guided ventilation and those for whom standardized ventilation parameters were used. Future studies should investigate the impact of hyperventilation and $ETCO_2$ monitoring on the outcome for patients with traumatic brain injury.

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