

Chapter 4. Resuscitation of blood pressure and oxygenation and prehospital brain-specific therapies for the severe pediatric traumatic brain injury patient

I. RECOMMENDATIONS

A. Standards. There are insufficient data to support a treatment standard for this topic.

B. Guidelines. Hypotension should be identified and corrected as rapidly as possible with fluid resuscitation. In children, hypotension is defined as systolic blood pressure below the fifth percentile for age or by clinical signs of shock. Tables depicting normal values for pediatric blood pressure by age are available (1). The lower limit of systolic blood pressure (5th percentile) for age may be estimated by the formula: $70 \text{ mm Hg} + (2 \times \text{age in years})$ (2). Evaluation for associated extracranial injuries is indicated in the setting of hypotension.

C. Options. Airway control should be obtained in children with a Glasgow Coma Score ≤ 8 to avoid hypoxemia, hypercarbia, and aspiration. Initial therapy with 100% oxygen is appropriate in the resuscitation phase of care. Oxygenation and ventilation should be assessed continuously by pulse oximetry and end-tidal CO_2 monitoring, respectively, or by serial blood gas measurements.

Hypoxia (defined as apnea, cyanosis, $\text{PaO}_2 < 60\text{--}65 \text{ mm Hg}$, or oxygen saturation $< 90\%$) should be identified and corrected rapidly. Hypoventilation (defined as ineffective respiratory rate for age, shallow or irregular respirations, frequent periods of apnea, or measured hypercarbia) is also an indication for airway control and assisted ventilation with 100% oxygen in the resuscitation phase of care.

Blood pressure should be monitored frequently and accurately. Timely fluid administration should be provided to maintain systolic blood pressure in the normal range. Charts with normal values based on age are available (1). Median (50th percentile) systolic blood pressure

for children older than 1 yr may be estimated by the formula: $90 + (2 \times \text{age in years})$ (2).

Sedation, analgesia, and neuromuscular blockade can be useful to optimize transport of the patient with traumatic brain injury (TBI). The choice of agents and timing of administration are best left to local Emergency Medical Services protocols.

The prophylactic administration of mannitol is not recommended. Mannitol may be considered for use in euvoletic patients who show signs of cerebral herniation or acute neurologic deterioration.

Mild prophylactic hyperventilation is not recommended. Hyperventilation may be considered in patients who show signs of cerebral herniation or acute neurologic deterioration, after correcting hypotension or hypoxemia.

D. Indications from the Adult Guidelines. In the adult guidelines for the prehospital management of severe TBI (3, 4), specific age-dependent ventilatory rates were provided as shown in Table 1.

II. OVERVIEW

In TBI literature on both children and adults, there is a growing understanding of the extreme sensitivity of the injured brain to secondary insults, both systemic and intracranial (3, 5–15). Secondary systemic insults are common in pediatric severe TBI. The systemic secondary insults that appear to have the most impact on outcome are hypoxia and hypotension.

The adult neurosurgical literature has traditionally defined hypotension as systolic blood pressure $< 90 \text{ mm Hg}$. In children, hypotension can be defined as less than the 5th percentile of normal systolic blood pressure for age. However, it should be emphasized that hypotension is a late sign of shock in children. Pediatric patients may maintain their blood pres-

sure despite significant hypovolemia and clinical signs of shock. Signs of decreased perfusion include tachycardia, loss of central pulses, decreased urine output below $1 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$, or increased capillary filling time of $> 2 \text{ secs}$.

In children, fluid resuscitation is indicated for clinical signs of decreased perfusion even when an adequate blood pressure reading is obtained. Shock is almost never due to head injury alone; evaluation for internal or spinal cord injury is indicated (16). Fluid restriction to avoid exacerbating cerebral edema is contraindicated in the management of the head-injured child in shock (17). If peripheral vascular access is difficult in children, intraosseous infusion of fluids and medications is indicated (18).

Apnea and hypoventilation are common in pediatric severe TBI. As in adults, hypoxia may be defined by $\text{PaO}_2 < 60\text{--}65 \text{ torr}$ or oxygen saturation $< 90\%$. However, hypoxia develops more rapidly in the child than in the adult during apnea or hypoventilation (19). Central cyanosis is neither an early nor a reliable indicator of hypoxemia in children. Also, adequate oxygenation does not necessarily reflect adequate ventilation. Respiratory rate and effort should be monitored and corrected to age-appropriate parameters.

III. PROCESS

We searched Medline and Healthstar from 1966 to 2001 by using the search strategy for this question (see Appendix A) and supplemented the results with literature recommended by peers or identified from reference lists. Of 133 potentially relevant studies, eight were used as evidence for this question (Table 2).

IV. SCIENTIFIC FOUNDATION

The negative impact of hypoxia and hypotension on the outcome of severe

Table 1. Age-dependent ventilatory rates (breaths/min) for eucapnea and hyperventilation

| Age | Rate for Eucapnea | Rate for Hyperventilation |
|----------|-------------------|---------------------------|
| Adults | 10 | 20 |
| Children | 20 | 30 |
| Infants | 25 | 35 |

TBI has been demonstrated repeatedly in studies of mixed adult and pediatric populations (3, 6, 7, 12–14). In these studies, hypoxia, hypercarbia, and hypotension were common and correlated with increased morbidity and mortality rates.

Hypoxia

Pigula et al. (10) analyzed the influence of hypoxia and hypotension on mortality from severe TBI (Glasgow Coma Scale ≤ 8) in two prospectively collected pediatric (age ≤ 16 yrs) databases. Hypoxia was defined as an emergency department admission $\text{PaO}_2 \leq 60$ mm Hg. For both the single-center database ($n = 58$) and the multiple-center database ($n = 509$, including the 58 from the single center), the presence of hypoxia alone did not significantly alter mortality rate. The combination of hypotension and hypoxia only slightly (and not significantly) increased the mortality rate over hypotension alone. It was concluded that hypotension is the most influential secondary insult determining short-term mortality rate. Hypotension with or without hypoxia was associated with mortality rates approaching those found in adults. Neither the degree nor the duration of hypoxia was quantified. The participating centers were well-developed pediatric trauma centers. As such, the apparent diminution in the effect of hypoxia on outcome might partially reflect the increased availability of effective airway management protocols for the prehospital situation.

Michaud et al. (20) found that level of oxygenation was associated with both mortality rate and the severity of disability of survivors. Concurrent chest injuries were strongly associated with increased mortality and morbidity rates. Children with PaO_2 levels between 105 and 350 mm Hg had significantly worse outcomes than those with $\text{PaO}_2 > 350$ mm Hg.

In a prospective study of 200 children, Mayer and Walker (21) found that mor-

tality rate was 55% in the presence of hypoxia, hypercarbia, or hypotension and only 7.7% without any of these factors present ($p < .01$). In a prospective cohort study by Ong et al. (22) in Kuala Lumpur, the presence of hypoxia increased the probability of a poor outcome by two- to four-fold. In the setting of abusive head trauma, Johnson et al. (23) found that apnea was present in the majority of patients and 50% were also hypotensive. It was concluded that cerebral hypoxia and/or ischemia was more strongly associated with poor outcome than mechanism of injury.

Resuscitation of Blood Pressure

Five studies directly addressed the influence of early hypotension on outcome from TBI. The impact of hypertension on survival was also addressed in two studies.

In the aforementioned study by Pigula et al. (10), they reported an 18% incidence of hypotension (defined as either a systolic blood pressure ≤ 90 mm Hg or a systolic blood pressure ≤ 5 th percentile for age) on arrival to the emergency department. A mortality rate of 61% was associated with hypotension on admission vs. 22% among patients without hypotension. When hypotension was combined with hypoxia, the mortality rate was 85%. Hypotension was a statistically significant predictor of outcome with a positive predictive value of 61%. Early hypotension negated the improvement in survival from severe TBI that is generally afforded by youth.

Kokoska et al. (24) performed a retrospective chart review of all pediatric patients admitted to a single level 1 trauma center over a 5-yr period. They limited their patient populations to children with nonpenetrating TBI with postresuscitation age-adjusted Glasgow Coma Scale scores between 6 and 8 ($n = 72$). They indexed secondary insults occurring during transport to the emergency department up through the first 24 hrs in the intensive care unit. Hypotension was defined as ≥ 5 min at or below the 5th percentile for age according to the Task Force on Blood Pressure Control in Children (1). The majority of hypotensive episodes occurred during resuscitation in the emergency department (39%) and the pediatric intensive care unit (37%). Patients left with moderate and severe disability had significantly more hypotensive episodes than those with good outcomes.

Michaud et al. (20) found that hypotension in the field and emergency department was significantly related to mortality rate in children. In a data bank study from four centers, Levin et al. (25) found that outcome was poorest in patients 0–4 yrs old, which was the group that demonstrated high rates of hypotension (32%).

In a prospective series of 6,908 adults and 1,906 children < 15 yrs of age at 41 centers, Luerssen et al. (26) found that hypotension was significantly associated with higher mortality rates in children. They reported a greater deleterious effect of hypotension in children than adults. Notably, children with severe hypertension had the lowest mortality rate.

In a recent retrospective study, White et al. (27) found that odds of survival in severe pediatric TBI increased 19-fold with maximum systolic blood pressure > 135 mm Hg, also suggesting that supranormal blood pressures are associated with improved outcome. In contrast, previous retrospective studies (28, 29) correlated early arterial hypertension with a worse neurologic outcome.

Brain Injury Specific Treatments in Prehospital Management

There is no evidence specifically dealing with the efficacy of any of the key brain-directed prehospital therapies, including sedation and neuromuscular blockade, mannitol, hypertonic saline, or hyperventilation on the outcome from severe pediatric TBI. The scientific foundation for the in-hospital use of these agents is discussed in separate sections of this document. Extrapolation of their use to the prehospital setting may be appropriate and is provided by consensus at the level of options in the recommendations section.

Key Elements From the Adult Guidelines Relevant to Pediatric TBI

The evidence-based review of the literature on prehospital airway, breathing, and ventilation management in the adult TBI population published as the *Guidelines for Pre-Hospital Management of Traumatic Brain Injury* (4) produced two class II studies (6, 7) demonstrating that prehospital hypoxia has a statistically significant negative impact on outcome. These studies led to the following recommendation, “Hypoxemia (apnea, cyanosis,

Table 2. Evidence table

| Reference | Description of Study | Data Class | Conclusion |
|-----------------------------|---|------------|---|
| Johnson et al. (23), 1995 | Retrospective medical record and imaging review of 28 children with confirmed child abuse with significant head injury (75% male, 50% age <3 mos, stratified GCS). Those with GCS 3–8 included five shaken, seven impact injuries. Presence of fracture, GCS, SAH, SDH, contusion, DBS, IVH, apnea, intubation, early seizure, retinal hemorrhage, and outcome were noted. Analysis: Two-way tables with Fisher's exact test for categorical and Cochran-Mantel-Haenszel test for ordinal. Significance at $p < .05$. | III | No patient with clinical evidence of cerebral hypoxia and/or ischemia had a good outcome. Trauma-induced apnea causes cerebral hypoxia, which is more fundamental to outcome than mechanism of injury. |
| Kokoska et al. (24), 1998 | Retrospective chart review, 1990–95 level I, single center, 72 children (3 mos–14 yrs 6 mos) GCS 6–8. Measures: age, gender, mechanism, injury type, duration ventilation and length of stay. Presence of hypoxia, hypotension, or hypercarbia during transport, ED, OR, and first 24 hrs in PICU. Analysis: ANOVA on continuous data. χ^2 or Fisher's exact test for nominal data. $p < .05$ was significant. Ages: 0–4 yrs, 5–9 yrs, and >10 yrs Transport time in 15-min intervals. | III | 97% survival. Early hypotension linked to prolonged length of stay and worse 3-month GOS. |
| Levin et al. (25), 1992 | Prospective databank cohort study of 103 children (<16 yrs) with severe TBI (GCS <9) at four centers. Patients received CT scan and ICP monitoring "treatment protocol." Hypotension was defined as below the age-dependent lower limit of normal systolic blood pressure. Measures: age, race, gender, mechanism, time to center, worst GCS, median ICP, pupillary reactivity, hypoxia, shock, mass lesion, skull fracture, GOS at 6 mos (86%) and 1 yr (73%). Analysis: mean/SD, box plots, logistic and linear regression. | III | Outcome was poorest in 0–4 yrs age group, which had an increased incidence of evacuated subdural hematomas (20%) and hypotension (32%). 14–21% in all age ranges were hypoxic. |
| Luerssen et al. (26), 1988 | Prospective series of 8,814 adult and pediatric TBI patients admitted to 41 metropolitan hospitals in NY, TX, and CA in 1980–81. 21.6% pediatric TBI patients (1,906 <15 yrs) compared with adult TBI patients (6,908 >15 yrs). Measures: age, gender, admission vital signs, injury mechanism, GCS post resuscitation, pupillary response, associated injury/AIS, "major symptoms," brain injury by imaging or at surgery, and mortality rate before hospital discharge. Hypoxia not studied. Profound hypotension: systolic BP 30 mm Hg below median for age. Analysis: Two-by-two tables by Pearson's χ^2 test with Yates correction. Ordered contingency tables by Mantel-Haentzel. Logistic regression for age vs. survival. | II | Only hypotension was associated with higher mortality rate in children. Children with severe hypertension had the lowest mortality rate. Both hypotension and hypertension were associated with higher adult mortality rate. Pediatric mortality rate was significantly lower than adult mortality rate, with notable exceptions of children with profound hypotension (33.3% <15 yrs vs. 11.8% >15 yrs) or subdural hematoma (40.5% <15 yrs vs. 43.9% >15 yrs). Age, even within the pediatric age group, is a major independent factor affecting TBI mortality. |
| Mayer and Walker (21), 1985 | Prospective study (1978–1981) of 200 consecutive children (3 wks–16 yrs, mean 5.6 yrs) with severe TBI (GCS <8). 124 male 76 female 43% IHI 57% HI/Mt Measures: age, GCS, mass lesions, oculovestibular reflexes, pupils, ICP, apnea, hypotension, hypoxia ($PO_2 < 60$), hypercarbic (>35 torr), multiple trauma, MISS score. Interventions: ICP monitor for GCS <6, GCS 6, 7, and abnormal CT. ICP >20 (79%) received hyperventilation (PCO_2 25–28 torr), diuretic, and barbiturate protocol. Analysis: χ^2 . | III | Mortality rate 21.5% IHI 10.5% HI+MT 30% 33% fixed dilated pupils 29% hypotension, hypercarbia, or hypoxia 28% altered OVR 26% mass lesions Mortality rate 55% with any hypotension, hypercarbia, or hypoxia vs. 7.7% without. 88% of HI+MT group had hypotension, hypercarbia, or hypoxia. GCS <4, increased ICP, MISS <25, hypotension, hypoxia, hypercarbia significant ($p < .01$) for poor outcome. |
| Michaud et al. (20), 1992 | Retrospective study of prospectively collected Trauma Registry data in 75 children presenting to Harborview Medical Center with severe TBI (GCS \leq 8) between January 1, 1985, and December 31, 1986. Mean 8.2 yrs; 67% male; 16% <2 yrs; 65% 3–14 yrs; 19% >14 yrs. Assessed fatality rate in system with advanced EMS and regional trauma center (83% received EMS field care). Identified factors predictive of survival and/or disability. GOS at discharge from acute care hospital measured. EMS, ED, hospital, autopsy records analyzed. Analysis: SPSS; logistic regression with EGRET; χ^2 or Fisher's exact test statistical significance; $p \leq .05$. | II | 33% fatality rate 60% associated injuries 86% intentional injuries fatal Mortality rate increased if hypotension or abnormal pupils noted in the field. ISS and pupillary reactivity predicted survival; 72-hr motor GCS and ED PO_2 predicted disability. ED $PO_2 > 350$ better outcome; PO_2 105–350 same outcome as hypoxic group. |

Table 2. (Continued)

| Reference | Description of Study | Data Class | Conclusion |
|--------------------------|---|------------|--|
| Ong et al. (22), 1996 | Prospective cohort study of 151 consecutive children (<15 yrs) admitted within 24 hrs of head injury (GCS <15) from 1993 to 1994 in Kuala Lumpur. Age groups: 0–4 yrs (n = 51); 5–9 yrs (n = 55); 10–14 yrs (n = 45). Stratified GCS 3–5; 6–8 Measured; age, gender, GCS admit and 24-hr, pupils, motor response, deficits, major extracranial injury, mass lesion, skull fracture, hypotension, and hypoxia. Follow-up GOS at discharge and 6 mos. Analysis: χ^2 for categorical variables. Student's <i>t</i> -test for continuous variables, association clinical/radiological factors, and outcome. Logistic regression for combination of factors to predict poor outcome. | II | Poor outcome related to GCS <8, abnormal pupils, motor deficits, hypoxia, hypotension, and extracranial injury. Hypoxia increases poor outcome by two- to four-fold in severe TBI. Five independent factors predict poor outcome: GCS at 24 hrs hypoxia on admission SAH DAI brain swelling on CT |
| Pigula et al. (10), 1993 | Five-yr prospective cohort study of 58 children (<17 yrs) and a matched set of 112 adults with severe TBI (GCS <8). Group I—normal BP and PaO ₂ . Group II—hypotension or hypoxia or both. Adults compared to this subgroup. ABG, BP, GCS, ISS, PaO ₂ , age on admission, and survival were measured. Analysis: Outcome by two-tailed χ^2 , Fisher's exact test, and ANOVA with Bonferroni's adjusted <i>t</i> -test. Statistical significance <i>p</i> ≤ .05. | II | Hypotension with or without hypoxia causes significant mortality rate in children compared with levels found in adults (<i>p</i> = .9). Adequate resuscitation probably the single most critical factor for optimal survival. Survival increased four-fold with neither hypoxia nor hypotension compared with either hypoxia or hypotension (<i>p</i> < .001). When added cohort to NPTR/509 children: Hypotension increased mortality rate even without hypoxia (<i>p</i> < .00001). If both hypoxia and hypotension present, only slightly increased mortality rate than with hypotension alone (<i>p</i> = .056). |

GCS, Glasgow Coma Scale; SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage; DBS, diffuse brain swelling; IVH, intraventricular hemorrhage; ED, emergency department; OR, operating room; PICU, pediatric intensive care unit; ANOVA, analysis of variance; GOS, Glasgow Outcome Scale; TBI, traumatic brain injury; CT, computed tomography; ICP, intracranial pressure; AIS, Abbreviated Injury Severity; BP, blood pressure; IHI, isolated head injury; HI, head injury; MT, multiple trauma; MISS, Modified Injury Severity Scale; OVR, oculovestibular reflexes; ISS, Injury Severity Score; EMS, emergency medical service; DAI, diffuse axonal injury; ABG, arterial blood gas; NPTR, National Pediatric Trauma Registry.

or arterial hemoglobin oxygen saturation [Sao₂] ≤90 mm Hg) must be avoided, if possible, or corrected immediately. When available, oxygen saturation should be monitored on all patients with severe TBI as frequently as possible or continuously. Hypoxemia should be corrected by administering supplemental oxygen." Issues specifically pertaining to the management of airway are addressed in Chapter 3.

The "Guidelines for the Management of [Adult] Severe Traumatic Brain Injury" (3) and the *Guidelines for Pre-Hospital Management of Traumatic Brain Injury* (4) produced class II (6, 7, 27, 30, 31) and class III (32–37) evidence from the adult literature that early hypotension is a statistically significant and independent factor associated with worsening outcome from TBI. From the evidence report on prediction of outcome from TBI (38), hypotension was one of the five factors found to have a ≥70% positive predictive value for mortality. Despite the solid evidence of the negative influence of early hypotension on outcome from TBI, there is much less evidence that reducing or

preventing such secondary insults improves outcome.

Regarding the use of brain-specific therapies in the prehospital setting, the "Guidelines for the Management of [Adult] Severe Traumatic Brain Injury" (3) and the *Guidelines for Pre-Hospital Management of Traumatic Brain Injury* (4) collectively addressed the use of sedation, neuromuscular blockade, mannitol, and hyperventilation in managing severe TBI during the prehospital period. With respect to sedation and neuromuscular blockade, they found no studies dealing directly with the effects of prehospital use of these agents on outcome from severe TBI. It was recommended at the option level that "sedation, analgesia, and neuromuscular blockade can be useful to optimize transport of the head-injured patient. Because no outcome studies provide guidance on the use of these adjuncts, the timing and choice of agents are best left to local Emergency Medical Services (EMS) protocols." (4)

The adult guidelines suggested no support for the prehospital use of mannitol. However, in two studies deleteri-

ous effects were not reported. An equally acceptable alternative position would be that mannitol is an effective but potentially hazardous method of lowering intracranial pressure and that its use during the prehospital period should be specifically limited to the euvolemic patient with evidence of cerebral herniation (a definite decrease in the level of consciousness, motor posturing or flaccidity, or pupillary changes such as anisocoria or bilateral pupillary dilation). Prophylactic use cannot be supported.

The *Guidelines for Pre-Hospital Management of Traumatic Brain Injury* (4) found no studies of the effect on outcome of the use of hyperventilation during the prehospital period. Recommendations, based on adult studies of the influence of hyperventilation used during the in-hospital period on physiologic indexes and outcome, stated; "hyperventilation (20 bpm in an adult, 25 bpm in a child, and 30 bpm in an infant) is the first line of intervention in the patient with suspected cerebral herniation." (4) Prophylactic hyperventilation was not supported.

V. SUMMARY

The literature on the influence of hypoxia and hypotension on outcome from severe TBI in adults is fairly clear. Hypotension and hypoxia are serious, and potentially preventable, secondary insults that significantly increase the morbidity and mortality rates of TBI.

Unfortunately, there is minimal specific evidence to indicate that prehospital protocols effective in preventing or minimizing hypoxic and hypotensive insults improve outcome. Therefore, despite the use of multivariate statistics to attempt to control for such confounding, the possibility remains that some, most, or all secondary insults occurring during the prehospital period that are associated with poor recovery are simply manifestations of the severity of injury and are not treatable entities.

A similar argument may be made for the pediatric literature on hypotension. Decreases in systolic blood pressure below some threshold (*vide supra*) appear to be quantitatively associated with worsening of recovery. As such, despite the absence of treatment efficacy data, maximizing efforts directed at rapid and complete volume resuscitation, coupled with protocols to minimize volume loss, are most consistent with the present body of literature and should be strongly emphasized components of prehospital care.

The situation with respect to prehospital hypoxia in pediatrics is less clear. In contrast to the adult literature, the only study that looked at prehospital hypoxia in any detail found that the presence of hypoxia alone did not significantly alter mortality rate. Such a finding, if not simply an artifact, could reflect either an increased resistance of the pediatric population to hypoxic insults in the face of severe TBI or, alternatively, unquantified efficiency of the prehospital care providers in preventing or minimizing hypoxic insults in the setting of these studies. In general, it is believed that the pediatric brain recovers better than an adult brain from a given traumatic insult. Pigula et al. (10), however, stated that they believed the occurrence of a hypotensive episode eliminated the improvement in survival from severe TBI that is generally afforded by youth. If an improved resistance to hypoxia is responsible for the lack of a demonstrated adverse influence on outcome, it is unlikely that such resistance is absolute. Therefore, although it is not proper to suggest altering treat-

ment in the absence of specific data, it is certainly reasonable to recommend that the hypoxia avoidance/airway protection protocols afforded the patients studied by Pigula et al. (10) be set as a favorable example. Although these protocols were not specified, they did use a population from a pediatric trauma registry as a large part of their study cohort. Since such patients were treated by pediatric trauma centers, this population sample cannot be assumed to represent routine pediatric prehospital trauma care. As such, the article by Pigula et al. (10) would seem strong, albeit indirect, support for basic life support/advanced trauma life support and pediatric advanced life support protocols to be universally applied as a minimum.

There is no contributing scientific literature on the role of the prehospital administration of brain-specific therapies in improving outcome from pediatric TBI. For the same period in adults, there is no literature on neuromuscular blockade or hyperventilation, one study on a single sedative agent with very limited applicability to TBI, and two studies that indirectly address the prehospital administration of mannitol. As such, the *Guidelines for Pre-Hospital Management of Traumatic Brain Injury* base their recommendations on data from the in-hospital period and consensus opinion. In the absence of evidence that their recommendations should be specifically altered for the pediatric population, we have suggested that the adult guidelines be considered as the first line of approach. The one area where we differ in our approach is that of mannitol; the adult guidelines dispute its use, whereas we conclude that the absence of evidence for or against this agent is more consistent with the stance that mannitol is an effective but potentially hazardous method of lowering intracranial pressure and that its use during the prehospital period should be specifically limited to the euvoletic patient with evidence of cerebral herniation. Prophylactic use cannot be supported.

The presence of hypoxia or hypotension after severe TBI in children increases morbidity and mortality rates. Specific threshold values for ideal levels of oxygenation and blood pressure support in the pediatric age group have not been clearly defined. Guidelines are warranted to support avoidance or rapid correction of systolic blood pressure less than the second standard deviation of normal for

Resuscitation and stabilization of the cardiovascular and respiratory systems in the field, during transfer, and in the hospital need to be emphasized in an effort to optimize outcome from severe pediatric brain injury.

age or of clinical signs of shock, apnea or hypoventilation, cyanosis, oxygen saturation <90%, or Pao₂ <60 mm Hg in children with severe head injury.

Early control of the airway and recognition and treatment of associated extracranial injuries are indicated. Despite endotracheal intubation, head-injured children remain at high risk for hypoxemia, hypercarbia, and major airway complications (39). The frequency of complications in airway procedures supports the use of protocols including medications for cerebral protection, anesthesia, pain control, and paralysis (40).

The "golden hour" clearly begins at the time of trauma. Although it is recognized that the field care of any trauma patient is encumbered both by the nature of the injury as well as by the often unfavorable and sometimes hostile environment in which it is encountered, it is apparent that whatever function is compromised by secondary insults during that period is generally not amenable to full recovery. It is therefore critical to optimize the prehospital care of the TBI patient. Ideally, this would be realized by bringing hospital-type care to the accident scene. Given the enormous variability of the early posttrauma period and the generally challenging environment in which care must be delivered, such a concept is not realistic. Indeed, the very concept itself continues to be the topic of raging debate (the "scoop and run" versus "stay and play" controversy). As such, it is expedient to simply select what seem to be the most salient points of prehospital TBI management and address them in an evidence-based fashion.

The goal of initial resuscitation in both adults and children is to prevent

secondary brain injury by restoring oxygenation, ventilation, and perfusion. Resuscitation and stabilization of the cardiovascular and respiratory systems in the field, during transfer, and in the hospital need to be emphasized in an effort to optimize outcome from severe pediatric brain injury.

VI. KEY ISSUES FOR FUTURE RESEARCH

Unfortunately, there is a lack of pediatric studies on the ability of protocols directed at minimizing or preventing hypotensive episodes to improve outcome from TBI. Therefore, the link between the predictive value of hypotension in predicting outcome and the treatment value of preventing hypotension in improving outcome, albeit logical, remains conjectural.

Hypotension

The determination of treatment thresholds for hypotension is not amenable to randomized controlled trials for ethical reasons. As such, it is necessary to address this issue by using large, prospectively collected observational databases that allow analysis of this variable while controlling statistically for confounding variables. It has also been suggested that supranormal blood pressures may be acceptable or even associated with improved outcome in children with severe traumatic brain injury. Further investigation in this area is also warranted.

Given the critical need to minimize or eliminate prehospital hypotensive episodes, randomized controlled trials addressing management protocols are necessary. Study of the timing, amount, and composition of resuscitation fluids to be used is warranted. Given the evidence on the efficacy of in-hospital administration of hypertonic saline plus the adult data supporting its use in the prehospital care of the adult TBI patient, a formal study of hypertonic prehospital resuscitation in pediatric TBI should be considered.

Hypoxia

Given the unclear nature of the pediatric literature on prehospital hypoxia, the first order of research should be to further define the nature of its occurrence and influence on outcome. Studies are needed with sufficient patient populations that have the statistical power to make definitive statements. The level of oxygenation during this period needs to

be accurately and repeatedly measured (such as by serial monitoring of peripheral oxygen saturation in the field) to address the influence of thresholds of magnitude and duration of hypoxia. This would allow us to assess the role of prehospital hypoxia on outcome as well as to accurately compare the efficacy of various management methods. Finally, since morbidity rate is generally believed to be more relevant to measuring outcome from hypoxic insults than mortality rate, we need to use functional recovery measures as our dependent variables in such investigations.

The effect of hypercarbia, with or without hypoxemia, on outcome is also not clearly defined and deserves investigation. Potential use of more aggressive oxygenation variables in the resuscitation period deserves further investigation.

Brain-Specific Treatments in the Prehospital Setting

The absence of pediatric literature in this area is striking. Clearly, we need to accomplish quantitative evaluation of various methods of managing the pediatric patient with suspected TBI. Comparative studies of different approaches to patient sedation are fundamental to every aspect of managing such patients. Similar studies regarding the use of hyperventilation and mannitol are also required. Although agent-specific, controlled studies would be optimal, a large, multiple-center prospective observational study might be a reasonable first-order approach.

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APPENDIX: LITERATURE SEARCH STRATEGIES

SEARCHED MEDLINE AND HEALTHSTAR FROM 1966 TO 2001

Chapter 4. Resuscitation and Prehospital Brain-Specific Therapies: Strategy A—Resuscitation of Blood Pressure and Oxygenation

1. exp craniocerebral trauma/
2. head injur\$.tw.
3. brain injur\$.tw.
4. 1 or 2 or 3
5. exp anoxia/ or “hypoxia”.mp.
6. exp hypotension/ or “hypotension”.mp.
7. 5 or 6
8. 4 and 7
9. limit 8 to (newborn infant <birth to 1 month> or infant <1 to 23 months> or preschool child <2 to 5 years> or child <6 to 12 years> or adolescence <13 to 18 years>)

Strategy B—Integration of Brain-Specific Treatments Into the Initial Resuscitation of the Severe Head Injury Patient

1. exp craniocerebral trauma/
2. head injur\$.tw.
3. brain injur\$.tw.
4. 1 or 2 or 3
5. exp analgesia/ or exp analgesics, opioid/ or exp “hypnotics and sedatives”/ or Midazolam/ or Propofol/ or “sedation”.mp.
6. neuromuscular blockade/ or “neuromuscular blockade”.mp.
7. exp resuscitation/ or “resuscitation”.mp.
8. “ACUTE CARE”.mp.
9. exp emergency medical services/ or “prehospital”.mp.
10. exp Ambulances/
11. exp intensive care units/
12. intensive care/ or “intensive care”.mp.
13. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. 4 and 13
15. limit 14 to (newborn infant <birth to 1 month> or infant <1 to 23 months> or preschool child <2 to 5 years> or child <6 to 12 years> or adolescence <13 to 18 years>)
16. limit 15 to english language