Pediatric Anesthesia 2008 **18**: 455–461 doi:10.1111/j.1460-9592.2008.02507.x

Review article

Management of critically ill children with traumatic brain injury

GILLES A. ORLIAGUET MD PhD, PHILIPPE G. MEYER MD AND THOMAS BAUGNON MD

Département d'Anesthésie – Réanimation et SAMU de Paris, Hôpital Necker Enfants Malades, AP-HP, Université Paris Descartes, Paris, France

Summary

The management of critically ill children with traumatic brain injury (TBI) requires a precise assessment of the brain lesions but also of potentially associated extra-cranial injuries. Children with severe TBI should be treated in a pediatric trauma center, if possible. Initial assessment relies mainly upon clinical examination, trans-cranial Doppler ultrasonography and body CT scan. Neurosurgical operations are rarely necessary in these patients, except in the case of a compressive subdural or epidural hematoma. On the other hand, one of the major goals of resuscitation in these children is aimed at protecting against secondary brain insults (SBI). SBI are mainly because of systemic hypotension, hypoxia, hypercarbia, anemia and hyperglycemia. Cerebral perfusion pressure (CPP = mean arterial blood pressure – intracranial pressure: ICP) should be monitored and optimized as soon as possible, taking into account age-related differences in optimal CPP goals. Different general maneuvers must be applied in these patients early during their treatment (control of fever, avoidance of jugular venous outflow obstruction, maintenance of adequate arterial oxygenation, normocarbia, sedation–analgesia and normovolemia). In the case of increased ICP and/or decreased CPP, first-tier ICP-specific treatments may be implemented, including cerebrospinal fluid drainage, if possible, osmotic therapy and moderate hyperventilation. In the case of refractory intracranial hypertension, second-tier therapy (profound hyperventilation with $P_aCO_2 < 35$ mmHg, high-dose barbiturates, moderate hypothermia, decompressive craniectomy) may be introduced, after a new cerebral CT scan.

Severe traumatic brain injury (TBI) is a life-threatening circumstance that requires specific management beginning as early as possible. This management requires a precise assessment of the brain lesions, as well as of any associated extra-cranial injuries. One of the major goals of critical care management in these children is aimed at protecting against secondary brain insults (SBI) (1), which represent a major cause of worsening in neurological outcome (1,2).

Correspondence to: G.A. Orliaguet, MD, PhD, Département d'Anesthésie – Réanimation et SAMU de Paris, Hôpital Necker Enfants Malades, AP-HP, Université Paris Descartes, 149, rue de Sèvres, 75743 Paris cedex 15, France (email: gilles.orliaguet@nck.ap-hop-paris.fr).

Table 1
Modified Glasgow Coma Scale for infants and children (3)

	Score	*Infant/nonverbal child*	*Verbal child/adult*
Eye opening	4	Spontaneously	Spontaneously
	3	To speech	To verbal command
	2	To pain	To pain
	1	No response	No response
Best motor response	6	Normal spontaneous movement	Obeys command
	5	Withdraws to touch	Localizes pain
	4	Withdraws to pain	Flexion withdrawal
	3	Abnormal flexion (decorticate)	Abnormal flexion (decorticate)
	2	Extension (decerebrate)	Extension (decerebrate)
	1	No response	No response

		< 2 years	*2–5 years*	*>5 years*
Best verbal response	5	Cries appropriately, coos	Appropriate words	Oriented
	4	Irritable crying	Inappropriate words	Confused
	3	Inappropriate screaming/crying	Screams	Inappropriate
	2	Grunts	Grunts	Incomprehensible
	1	No response	No response	No response

Assessment of critically ill children with a TBI

The evaluation of critically ill children with TBI begins with a clinical examination. Then, some additional examinations are performed to evaluate more precisely the consequences of the TBI. These examinations include transcranial Doppler (TCD), CT scan, arterial and intracranial pressure monitoring, and magnetic resonance imaging (MRI) in some cases.

Clinical assessment

A thorough neurological examination must be performed as soon as the child is clinically stable, as it will serve of reference for future assessments (3). In life-threatening situations, evaluation of the level of neurological distress relies only upon the determination of the pediatric Glasgow Coma Scale (GCS) score (Table 1), evaluation of pupillary diameter and reactivity (Table 2), and examination of the brain stem reflexes. In less acute situations, the examination will also search for clinical evidence of increased intracranial pressure (ICP) and associated focal deficits (4). Moreover, there is a good correlation between the initial pediatric GCS and outcome (5). The analysis of the circumstances of the trauma is also important to determine the potential severity of the trauma. The kind of impact (pedestrian–vehicle crash, car crash, fall from height, etc.) and the associated circumstances (multiple victims, prolonged incarceration, etc.) may also indicate severe injuries. This notion is important because an initial reassuring GCS score could lead to an underestimation of the severity of the TBI. This underestimation might lead to the 'Talk and Die' scenario (6).

Table 2
Abnormal pupillary responses (3)

Pupillary finding	*Possible etiology*
Bilateral fixed and dilated pupils	Indicates inadequate CPP; may be irreversible
Bilateral myosis	Injury to pons; early central herniation; opioid administration
Unilateral fixed and dilated	Transtentorial herniation; traumatic optic nerve injury
Unilateral myosis	Horner's syndrome; unilateral brainstem injury
Hippus	May indicate irritation to occulomotor nucleus; can be normal variant

Standard radiography

Standard skull radiography is no longer recommended in children with TBI. On the other hand, TBI may be associated with C-spine injury, and coma may hide clinical symptoms of the spinal injury. Thus, lateral cervical spine X-ray is performed on admission of the patient, as well as chest and pelvic X-ray. Anyway, the body CT scan performed in a

stabilized child must also check the cervical, dorsal and lumbar spine.

CT scan

The radiological examination of choice for immediate assessment of the child with severe TBI is a noncontrast cerebral CT scan (3). In the case of life-threatening brain herniation, whatever the urgency for surgical intervention, this CT scan must be obtained with high-speed spiral imaging. In less acute situations, the need for radiological explorations must balance the risks and benefits of immediate explorations. It is wiser to spend enough time to adequately stabilize the cardio-respiratory status of the child before rushing to the CT scan, than to have to do it in the remote area of the radiology department (4). In children, the CT scan interpretation requires some specific knowledge, because of anatomical and physiological particularities. A CT scan performed too early following the traumatic accident may be falsely reassuring, explaining why it may be necessary to perform a new examination in case of neurological worsening. Nevertheless, a second routine scheduled head CT scan within 24–36 h after admission in pediatric patients with moderate or severe head trauma is unlikely to yield any change in therapy. Clinically and intracranial pressure-oriented CT scan enable a better selection of patients finally requiring changes in therapy, including surgery (7). Because severe TBI may frequently be associated with extra-cranial injuries, a contrast enhanced thoracic and abdominal CT scan is mandatory.

Transcranial Doppler ultrasonography

Transcranial Doppler ultrasonography (TCD) is a noninvasive monitor providing information on cerebral blood flow (CBF) and hemodynamics (8). Assessment of CBF velocities is usually performed in the middle cerebral arteries. The advantages of this technique are its noninvasive character, the possibility to monitor both sides, and the easy reproducibility of this examination. The obtained signal gives information about systolic, diastolic, and mean blood flow velocity. Under normal conditions, the diastolic velocity is about 40% of the systolic velocity. The cerebrovascular resistances are quantified by the Pulsatility Index (PI) [$PI = (FV_{sys} - FV_{dias})/FV_{mean}$]. In addition, the assessment of the morphology of the curve may give interesting information about the conditions of the cerebral hemodynamics (8). However, only few studies have evaluated the interest of TCD in children with severe TBI. Trabold *et.al* have demonstrated that an initial TCD has prognostic value (9). In this study, a diastolic velocity below 25 $cm{\cdot}s^{-1}$ on admission was associated with a bad neurological outcome (9).

Magnetic resonance imaging (MRI)

The sensibility of MRI is better than CT scan to detect contusion and brain swelling of the white substance, of the brain stem and of the spinal cord. However, MRI must be performed in a stabilized child, and therefore is usually done only when there is a discrepancy between clinical evaluation and CT scan imaging.

Intracranial pressure monitoring

Control of intracranial pressure (ICP) within the normal range is aimed at maintaining an adequate cerebral perfusion pressure (CPP) (1,10). All children with a GCS score of 8 or less after cardio-respiratory resuscitation, should benefit from ICP monitoring (1). Children with higher GCS scores but who exhibit evidence of worsening neurological status or with neuroimaging results suggesting intracranial hypertension must also benefit from ICP monitoring (1). A ventricular catheter connected to an external strain gauge is the most reliable method of monitoring ICP (1). It also allows therapeutic cerebrospinal fluid (CSF) drainage. However, there is a septic risk, proportionally increasing with the prolongation of ICP monitoring. In addition, it may be difficult to insert the catheter in the case of severe brain swelling with collapsed lateral ventricles. Parenchymal ICP monitoring with fiberoptic or strain gauge catheter tip transduction is similar to ventricular ICP monitoring, but has potential for measurement drift. Subarachnoid, subdural, epidural devices and externally placed anterior fontanel monitors are less accurate and should not be used (1). The effect of intracranial hypertension on outcome after severe TBI appears correlated with the absolute peak value

of ICP and the duration of intracranial hypertension. Several studies have shown that mortality increases with increased ICP and decreased CPP (10,11). Some authors advocate an ICP threshold for treatment of 20 mmHg for children aged 8 years, 18 mmHg for children aged 1–8 years and 15 mmHg for infants (12). ICP monitoring must be coupled with invasive arterial blood pressure measurement to calculate the cerebral perfusion pressure (CPP = mean arterial pressure - ICP). In children with severe TBI, it is recommended to maintain a CPP at least above 40 mmHg to prevent secondary ischemic brain insults (1). This guideline is in accordance with the results of a study by Downard *et al*. (13), showing an increased risk of death when CPP was less than 40 mmHg. However, one should theoretically take into account the age-related continuum for the optimal treatment threshold for CPP (14). In fact, as for ICP, there are also age-related differences in the specificity of CPP in relation to outcome. Therefore, it has been recommended to maintain CPP between 40 and 65 mmHg according to the age of the child (1). The results of a recent retrospective study are in accordance with this recommendation, showing that CPP of 53, 63 and 66 mmHg should be the minimum to strive for in children aged 2–6, 7–10 and 11–16 years respectively (11).

Critical care management

Although a precise assessment of a child with TBI is necessary to drive the treatment, management of severe brain insults must not be delayed. Treatment of critically ill children with TBI aims at protecting against secondary brain insults (SBI), which exacerbate neuronal damage and brain injuries. SBI are mainly due to systemic hypotension, hypoxia, hypercarbia, anemia and hyperglycemia. It has been suggested that an early (prehospital) and aggressive treatment, aimed at preventing and/or treating hypoxia, hypercarbia and hypotension could decrease mortality and improve neurological outcome after severe TBI in children (2). There is also a relationship between age-appropriate systolic blood pressure (AASBP) percentile and outcome after severe pediatric TBI (15). In a recent study, AASBP <75th percentile was associated with poor outcome after severe pediatric TBI, even when SBP was superior or equal to 90 mm Hg (15). Therefore, systolic blood pressure must be maintained at least over 90 mmHg; however, it may be not enough, especially in older children.

The acknowledged negative influence of SBI on outcome promotes cardio-respiratory resuscitation as the cornerstone upon which treatment of severe TBI must be based (1). Thus, in the lack of obvious evidence of elevated ICP, management must aim at optimizing circulation, ventilation and oxygenation. Alternatively, signs of transtentorial herniation are strong evidence of intracranial hypertension and should initiate rapid treatment to lower ICP. Under such circumstances, it is necessary to reassess the balance of cerebral and systemic priorities for the individual situation.

Intracranial hypertension and CPP management

Uncontrolled increased ICP is very deleterious and must be aggressively treated as soon as possible to reduce cerebral ischemia and prevent definitive after-effects. In this setting, the goal of any therapy is to lower ICP enough to increase CPP and improve cerebral oxygenation.

General maneuvers

First, general maneuvers are applied, including: treatment of fever, avoidance of jugular venous outflow obstruction, maintenance of normovolemia, normoxia and normocarbia ($P_aCO_2 \geq 35$ mmHg), preservation of adequate sedation–analgesia. Mechanically ventilated children with acute TBI should be adequately sedated and have an optimal pain release to avoid anxiety and pain, that in turn may increase ICP. An appropriate sedation should also facilitate adaptation to mechanical ventilation. The most common agents used are opioids and benzodiazepines. In children, prolonged sedation with propofol should be avoided because of the risk of metabolic acidosis and propofol infusion syndrome (16,17). Neuromuscular blocking agents must not be used systematically, but could be introduced in the case of difficult ventilation despite adequate sedation–analgesia (12). The cerebral effects of sedation and analgesia should always be titrated against the net effect on CPP (1), as for any therapeutic intervention. Thirty degree elevation and neutral head positioning may be used to decrease ICP in

normovolemic children, with CPP monitoring to assess safety and efficacy. In children, especially in case of associated extra-cranial injuries, severe TBI is often associated with hypovolemia-induced hypotension. Maintaining CPP requires optimization of mean arterial pressure (MAP) with fluid therapy and vasoactive drugs. When ICP remains elevated despite general maneuvers, first-tier ICP-specific treatment is used.

First tier ICP-specific treatments

CSF drainage. CSF drainage provides immediate but transient ICP decrease, and may be achieved with a ventriculostomy catheter (1). However, CSF drainage is rarely possible in children with severe TBI because edema and diffuse brain swelling are responsible for an obstruction of lateral ventricles. The next step is the use of hyperosmolar therapy.

Osmotic therapy. Osmotic agents are extensively used for management of intracranial hypertension. Mannitol (bolus doses of 0.5–1 $g \cdot kg^{-1}$ every 4–6 h) remains the cornerstone of those therapies, although mannitol has never been compared with placebo. In adults, its efficiency has been compared with other therapies aimed at decreasing ICP, and mannitol is as efficient, or even better, than CSF drainage. In children, there are little data on mannitol but a long-standing clinical use. Up to now, two short series and one randomized study have reported the use of hypertonic saline (HS) in children (18–20). In the randomized study, it was shown that the treatment of severe TBI with HS was superior to lactated Ringer's solution in children (19). In this study, children treated with HS require fewer interventions, have fewer complications, and stay for a shorter time in the ICU. In the case series, reported by Khanna *et al*(18), it was shown that an increase in serum sodium concentration significantly decreases ICP and increases CPP in severe TBI children with intracranial hypertension resistant to conventional therapy. In addition, sustained hypernatremia and hyperosmolarity were safely tolerated in these patients. At the present time, HS (continuous infusion of 3% HS, 0.1–1.0 $ml \cdot kg^{-1} \cdot h^{-1}$) has a limited clinical experience but reasonably good performance in contemporary clinical trials. There is no recommendation towards one or the other therapy (1,12).

Hyperventilation. Mechanical ventilation should provide adequate oxygenation (oxygen saturation >90%) and avoid hypercarbia ($P_aCO_2 > 38$ mmHg). In children, hypocarbia ($P_aCO_2 < 35$ mmHg) decreases cerebral blood flow and can induce cerebral ischemia (21). Thus, prophylactic hyperventilation should be avoided in children with TBI, while mild hyperventilation may be considered only in the case of intracranial hypertension refractory to general maneuvers, cerebrospinal drainage and hyperosmolar therapy (1).

Antiepileptic medication. Children are more prone to develop seizures than adults, because of a lower epileptogenic threshold. Therefore, monitoring should include either continuous EEG (if possible) or at least discontinuous but regular EEG monitoring. Prophylactic antiepileptic medications do not prevent late posttraumatic seizure and are not recommended. Nevertheless, treatment for clinical or subtle seizure must be quickly instituted after the diagnosis to improve the outcome (1).

Second tier therapy

Profound hyperventilation ($P_aCO_2 < 35$ mmHg). It may be used as a second-line therapy in the case of refractory intracranial hypertension. However, it requires cerebral blood velocities or oxygenation monitoring to detect cerebral ischemia (1).

Barbiturates. Systematic use of barbiturates is not recommended in all children with severe TBI. On the other hand, high-dose barbiturates may be used in the case of refractory intracranial hypertension (1). If high-dose barbiturate therapy is used, then appropriate hemodynamic monitoring and cardiovascular support are essential (1,12).

Moderate hypothermia. Hyperthermia (body temperature >38°C) is a known factor that may worsen outcome through several mechanisms (increasing metabolic demand, inflammatory changes, lipid peroxidation, neuronal excitoxicity, cell death, and acute seizure) and must be avoided. The concept of hypothermia for brain protection is based on the simple principle that cooling reduces the cerebral metabolic rate of oxygen consumption. Published data are rather controversial. Some authors have shown that hypothermia does not improve

outcomes (22), while others have demonstrated an ICP decrease with hypothermia (23). One study in children has demonstrated the safety of the method, but the effects on functional outcome and intracranial hypertension were not assessed (24). The only large study published on therapeutic hypothermia in severe TBI children has presented the results of the pretrial clinical evaluation phase of a large randomized multicenter study on moderate therapeutic hypothermia in severe TBI children (25). This study aimed at ensuring that compliance with complex hypothermia therapy and consensus-based clinical management guidelines of care were successfully implemented across the centers (25). Although some authors advocate mild hypothermia (32–34°C) within 6 h of TBI, there is no recommendation to use hypothermic strategy in children with severe TBI (1).

Surgery: Surgery is not a first-line treatment except to evacuate compressive subdural or epidural hematomas. Intracranial hypertension refractory to medical therapeutics may be treated by decompressive craniectomy (with duraplasty). However, only a selected population with specific criteria may benefit from this surgery: diffuse cerebral swelling, within 48 h of injury, no episodes of sustained ICP >40 mmHg, secondary clinical deterioration, and evolving cerebral herniation syndrome (1).

Strategy of assessment and management of the critically ill children with head injury

Assessment of critically ill children with head injury must be carefully but quickly performed and must not delay treatment. According to the clinical assessment and severity, the implementation of each treatment follows a strategy in which intracranial hypertension and CPP management play a central role. Following general maneuvers application, the first tier interventions are used and included: CSF drainage, osmotic therapy, prevention of seizures, and moderate hyperventilation. If these therapeutic interventions are not sufficient, after a new CT scan excluding any complications surgically curable, the next steps may include: profound hyperventilation, high-dose barbiturates, and/or decompressive craniectomy. All these procedures are summarized in Figure 1.

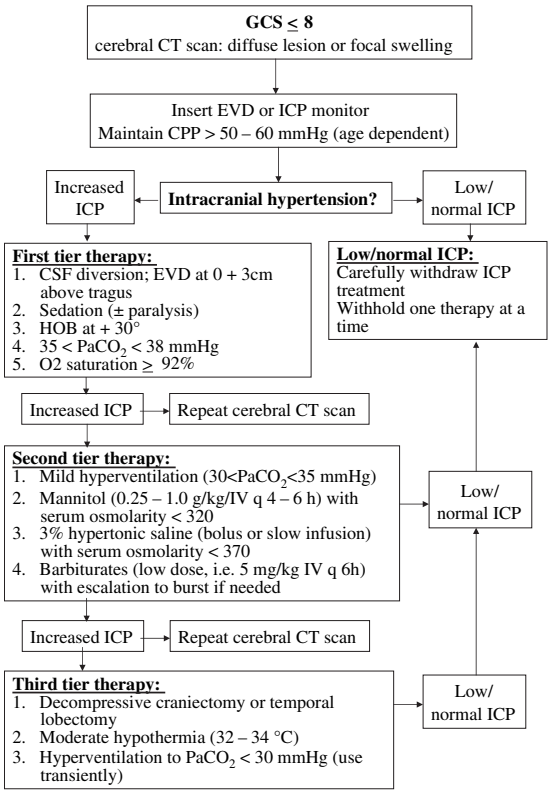

Figure 1
Algorithm for critical care management of head trauma children, adapted from Mazzola and Adelson (12). GCS, Glasgow coma scale; ICP, intracranial pressure; EVD, external ventricular drainage; CSF, cerebrospinal fluid; HOB, head of the bed.

Conclusion

The prevention of secondary brain injury is the aim of the management of TBI in children. Control of life-threatening problems by simple methods, such as cardiovascular resuscitation and mechanical ventilation, are the first and certainly the most effective steps. However, one should remember that children with severe TBI may also present associated extracranial injuries. A classical source of error is to focus only on a potential severe cerebral lesion while neglecting a bleeding abdominal lesion or underestimating the role of a pulmonary contusion in the respiratory distress. This is the reason why children with severe TBI should be transported directly to a pediatric trauma centre (if available), rather than to

the nearest available general hospital (1). In fact, there is a growing body of evidence suggesting that children with severe TBI are more likely to survive if treated in such specialized centers (1, 26).

References

1 Adelson PD, Bratton SL, Carney NA, Chesnut RM *et al*. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents. *Pediatr Crit Care Med* 2003; **4:** S1–S75.

2 Kokoska ER, Smith GS, Pittman T, Weber TR. Early hypotension worsens neurological outcome in pediatric patients with moderately severe head trauma. *J Pediatr Surg* 1998; **33:** 333–338.

3 Marcoux KK. Management of increased intracranial pressure in the critically ill child with an acute neurological injury. *AACN Clin Issues* 2005; **16:** 212–231.

4 Meyer P, Legros C, Orliaguet G. Critical care management of neurotrauma in children: new trends and perspectives. *Childs Nerv Syst* 1999; **15:** 732–739.

5 Keskil IS, Baykaner MK, Ceviker N, Kaymaz M. Assessment of mortality associated with mild head injury in the pediatric age group. *Childs Nerv Syst* 1995; **11:** 467–473.

6 Humphreys RP, Hendrick EB, Hoffman HJ. The head-injured child who ''talks and dies''. A report of 4 cases. *Childs Nerv Syst* 1990; **6:** 139–142.

7 Tabori U, Kornecki A, Sofer S, Constantini S *et al*. Repeat computed tomographic scan within 24–48 hours of admission in children with moderate and severe head trauma. *Crit Care Med* 2000; **28:** 840–844.

8 Orliaguet GA. Cerebral monitoring in children. *Pediatr Anesth* 2004; **14:** 407–411.

9 Trabold F, Meyer PG, Blanot S, Carli PA *et al*. The prognostic value of transcranial Doppler studies in children with moderate and severe head injury. *Intensive Care Med* 2004; **30:** 108–112.

10 Catala-Temprano A, Claret Teruel G, Cambra Lasaosa FJ, Pons Odena M *et al*. Intracranial pressure and cerebral perfusion pressure as risk factors in children with traumatic brain injuries. *J Neurosurg* 2007; **106:** 463–466.

11 Chambers IR, Stobbart L, Jones PA, Kirkham FJ *et al*. Age-related differences in intracranial pressure and cerebral perfusion pressure in the first 6 hours of monitoring after children's head injury: association with outcome. *Childs Nerv Syst* 2005; **21:** 195–199.

12 Mazzola CA, Adelson PD. Critical care management of head trauma in children. *Crit Care Med* 2002; **30:** S393–S401.

13 Downard C, Hulka F, Mullins RJ, Piatt J *et al*. Relationship of cerebral perfusion pressure and survival in pediatric brain-injured patients. *J Trauma* 2000; **49:** 654–658.

14 Chambers IR, Kirkham FJ. What is the optimal cerebral perfusion pressure in children suffering from traumatic coma? *Neurosurg Focus* 2003; **15:** E3.

15 Vavilala MS, Bowen A, Lam AM, Uffman JC *et al*. Blood pressure and outcome after severe pediatric traumatic brain injury. *J Trauma* 2003; **55:** 1039–1044.

16 Sabsovich I, Rehman Z, Yunen J, Coritsidis G. Propofol infusion syndrome: a case of increasing morbidity with traumatic brain injury. *Am J Crit Care* 2007; **16:** 82–85.

17 Vasile B, Rasulo F, Candiani A, Latronico N. The pathophysiology of propofol infusion syndrome: a simple name for a complex syndrome. *Intensive Care Med* 2003; **29:** 1417–1425.

18 Khanna S, Davis D, Peterson B, Fisher B *et al*. Use of hypertonic saline in the treatment of severe refractory posttraumatic intracranial hypertension in pediatric traumatic brain injury. *Crit Care Med* 2000; **28:** 1144–1151.

19 Simma B, Burger R, Falk M, Sacher P *et al*. A prospective, randomized, and controlled study of fluid management in children with severe head injury: lactated Ringer's solution versus hypertonic saline. *Crit Care Med* 1998; **26:** 1265–1270.

20 Fisher B, Thomas D, Peterson B. Hypertonic saline lowers raised intracranial pressure in children after head trauma. *J Neurosurg Anesthesiol* 1992; **4:** 4–10.

21 Skippen P, Seear M, Poskitt K, Kestle J *et al*. Effect of hyperventilation on regional cerebral blood flow in head-injured children. *Crit Care Med* 1997; **25:** 1402–1409.

22 Clifton GL, Miller ER, Choi SC, Levin HS *et al*. Lack of effect of induction of hypothermia after acute brain injury. *N Engl J Med* 2001; **344:** 556–563.

23 Biswas AK, Bruce DA, Sklar FH, Bokovoy JL *et al*. Treatment of acute traumatic brain injury in children with moderate hypothermia improves intracranial hypertension. *Crit Care Med* 2002; **30:** 2742–2751.

24 Adelson PD, Ragheb J, Kanev P, Brockmeyer D *et al*. Phase II clinical trial of moderate hypothermia after severe traumatic brain injury in children. *Neurosurgery* 2005; **56:** 740–754.

25 Hutchison J, Ward R, Lacroix J, Hebert P *et al*. Hypothermia pediatric head injury trial: the value of a pretrial clinical evaluation phase. *Dev Neurosci* 2006; **28:** 291–301.

26 Orliaguet G, Meyer P, Blanot S, Schmautz E *et al*. Validity of applying TRISS analysis to paediatric blunt trauma patients managed in a French paediatric level I trauma centre. *Intensive Care Med* 2001; **27:** 743–750.

Accepted 17 January 2008

