Medical management of severe traumatic brain injury

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This article reviews the current guidelines for the management of patients with severe traumatic brain injury from presentation in the accident and emergency department, through transfer, to specialist treatment in a neurocritical care unit.

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Head injury is a common condition dealt with by health-care workers from many professional groups. In the UK, approximately 1.4 million people attend accident and emergency (A&E) departments with a head injury each year. Approximately 20% of those require admission to hospital but only 2500 have severe head injury (Glasgow Coma Scale (GCS) score ≤8 out of 15). Although the incidence of head injury is high, the majority of this is minor and therefore the mortality rate is relatively low, accounting for only 7 deaths per 100 000 population (Jennett, 1996). This represents 1% of overall deaths, but 15% of deaths in the 15–45-year age group.

Put another way, less than 0.2% of people attending A&E departments with head injury have a fatal outcome; however, the incidence of significant morbidity, even in milder forms of injury, is higher than has previously been appreciated. Traumatic brain injury (TBI) is a huge socioeconomic problem because it affects mainly adults in their most productive years and contributes massively to the prevalence of long-term disability.

There have been marked improvements in the treatment of patients with severe TBI over the past decade, leading to a reduction in both mortality and morbidity. Advances in management have occurred in the pre-hospital setting, in the A&E department and in the intensive care unit. It is difficult, however, to state exactly which points of the management pathway have contributed most to improved outcome.

TABLE 1.
Causes of primary and secondary brain injury

Primary brain injury	Diffuse axonal injury	
	Haemorrhagic contusions and lacerations	
	Extradural haematoma	
	Subdural haematoma	
	Traumatic subarachnoid haemorrhage	
Secondary brain injury	Intracranial	Expanding haematomas
		Brain swelling
	Extracranial	Systemic hypotension
		Hypoxaemia
		Hypercapnia and hypocapnia
		Hyperthermia
		Disturbances of blood coagulation

PATHOPHYSIOLOGY OF SEVERE TRAUMATIC BRAIN INJURY

The head, being located at the top of a flexible spine, is prone to the effects of rapid acceleration and deceleration following impact. Neurones are subject to shearing forces and blood vessels may be torn, whereas the brain tissue itself may be damaged by bony prominences within the skull during violent movements. The result is a heterogeneous group of intracranial pathologies with the generic description of TBI.

Primary brain injury is the direct result of mechanical trauma applied at the moment of impact and causes irreversible cell damage from physical disruption of neurones or axons (*Table 1*). It cannot be treated by medical intervention, although early evacuation of expanding intracranial mass lesions reduces morbidity and mortality.

Secondary brain injury begins from the moment of primary traumatic injury and develops during the subsequent minutes, hours and days, causing further neuronal damage and worsening of the ultimate neurological deficit. It rep-

resents additional insults to the 'at-risk' neuronal tissue and is essentially ischaemic in nature. Secondary brain injury occurs as a result of a variety of intracranial and extracranial causes (*Table 1*), which can be manipulated by clinicians throughout its course.

Cerebral ischaemia is the dominant factor determining neurological outcome after severe TBI. It occurs when blood flow falls below a critical level, causing the delivery of oxygen and essential substrates to be insufficient for the brain's metabolic needs. Profound changes in cerebral blood flow (CBF) occur after TBI, and up to one third of patients sustain significant cerebral hypoperfusion in the first few hours after injury.

Blood vessels lose the ability to control their resistance in response to changes in perfusion pressure (pressure autoregulation), making blood flow dependent on systemic blood pressure and rendering the brain susceptible to damage at both high and low pressures. There may also be a loss of the normal vascular reactivity to arterial carbon dioxide tension ($PaCO_2$). Furthermore, acute intracranial injury initiates a cascade of ionic, metabolic and inflammatory changes that renders the brain particularly susceptible to secondary insults (Teasdale and Graham, 1998). All forms of secondary brain insults lead to a worse neurological outcome and are largely preventable or treatable (Maas et al, 1997).

RESUSCITATION AND STABILIZATION

Resuscitation after TBI is a key stage at which mortality and morbidity can be influenced. Two particular areas of intervention that improve outcome are rapid diagnosis and evacuation of expanding intracranial haematomas (Royal College of Surgeons, 1999), and the prevention of secondary brain injury by the correction of systemic hypoxaemia and hypotension (Chesnut, 1997).

More than one third of severely head-injured patients sustain either hypoxia or hypotension (or both) during the acute post-injury period, and this is associated with a doubling of mortality and a significant increase in morbidity (Chesnut, 1995). Initial management should therefore be directed toward the time-honoured resuscitation mantra of airway, breathing and circulation. A detailed secondary survey should be undertaken to identify other injuries. Life-threatening extracranial injuries should be treated before definitive neurosurgical treatment, but non-life-threatening injuries may simply be stabilized.

Airway management and ventilation

Patients with a severe TBI are unable to protect their airway because of a reduced level of consciousness. They also frequently have poor respiratory function and impaired gas exchange. Unconscious patients (GCS score <8) require early intubation and ventilation to maintain arterial oxygen tension (PaO_2) and $PaCO_2$ within normal ranges.

Protection of the cervical spine with manual in-line immobilization during intubation is essential because cervical spine injury is commonly associated with TBI. An oral endotracheal tube should be placed under direct laryngoscopy following an appropriate dose of an intravenous anaesthetic agent. The intracranial pressure (ICP) response to laryngoscopy is well maintained in the unconscious patient, so adequate anaesthesia is essential; however, the doses should be titrated to the patient's cardiovascular status.

It should be assumed that the patient has a full stomach, and a rapid sequence induction is mandatory with placement of an oro-gastric tube post-intubation in order to decompress the stomach and prevent gastric dilatation. The use of suxamethonium can be justified because the rise in ICP it produces is minimal and rapid, and full relaxation is essential for rapid airway control.

Once the airway has been secured, mechanical ventilation should be commenced to maintain PaO_2 at >13.5 kPa and $PaCO_2$ between 4.0 and 4.5 kPa (Maas et al, 1997). Sedation and paralysis should be maintained with short-acting agents to allow easy ventilation and prevent coughing in the presence of the endotracheal tube.

Cardiovascular resuscitation

Maintenance of normal or supranormal systemic blood pressure is crucial to optimize neurological outcome after severe TBI (Chesnut, 1997). During resuscitation, a mean arterial pressure (MAP) of >90 mmHg should be maintained (Maas et al, 1997) with intravenous fluids and inotropes. Closed head injury itself does not cause hypotension in adults, but the hypotensive effect of sedative agents often requires support with a modest dose of noradrenaline.

TRANSFER TO A NEUROSURGICAL UNIT

In the UK, patients with TBI are more likely to be admitted to hospitals with no neurosurgical facilities and, following diagnosis and resuscitation, require transfer to a specialist neurosurgical centre. Delay in providing definitive sur-

gical treatment is a major preventable cause of morbidity and mortality (Royal College of Surgeons, 1999). Criteria for transfer to a neurosurgical centre were previously based on deteriorating neurology, but it is now accepted that a more preventive strategy should be adopted.

The widespread use of computed tomography (CT) scanning has led to the revision of referral guidelines (Scottish Intercollegiate Guidelines Network, 2000; Gabriel et al, 2002) summarized in *Table 2*. All general hospitals should have well-established local guidelines (based upon national guidelines) agreed with their local neurosurgical centre. The use of computerized links for the transfer of CT images between centres dramatically reduces the time taken for diagnosis and referral.

The transfer of a severely head-injured patient requires careful planning, although time must be used efficiently so as not to delay urgent surgery. Appropriate emergency and monitoring equipment, drugs and infusion devices must be available for the journey. Staff who accompany the patient should have suitable training, skills and experience in resuscitation and intensive care medicine. It has been recommended that doctors undertaking transfer of head-injured patients should have undergone a minimum of 2 years training in an appropriate specialty (usually anaesthesia) and be of at least specialist registrar grade (Association of Anaesthetists of Great Britain and Ireland, 1996).

An appropriately trained assistant, usually an operating department practitioner or intensive care nurse, should accompany the patient throughout the transfer. Copies of notes, prescription charts, observation charts and CT scans must accompany the patient to the neurosurgical centre. Although it can be difficult to write in a moving vehicle, a record of the patient's clinical observations should be kept during the transfer.

NEUROSURGICAL INTENSIVE CARE MANAGEMENT

The primary goal of surgical treatment in severe TBI is the removal of a discrete haematoma (subdural and extradural) within 4 hours of injury (Royal College of Surgeons, 1999). The aim of intensive care management is to restore and maintain the brain's normal physiological environment in order to prevent or treat secondary ischaemic brain injury. Specialist neurocritical care with ICP and cerebral perfusion pressure (CPP) guided therapy should be available for all patients with severe TBI and is likely to improve outcome (Patel et al, 2002).

Monitoring

Systemic monitoring: Minimal monitoring requirements include electrocardiogram, pulse oximetry, invasive arterial blood pressure, urine output, temperature and end tidal carbon dioxide. Central venous pressure monitoring is essential to guide cardiovascular management; however, head-down tilt for central line insertion may exacerbate raised ICP and ultrasound guidance is particularly helpful in this group of patients. An oesophageal Doppler monitor or pulmonary artery flotation catheter can assist in the management of patients with cardiovascular instability. Regular blood glucose, serum electrolytes and arterial blood gas analysis are required to optimize physiological parameters.

Cerebral monitoring: Intracranial monitoring devices allow management strategies to be targeted to the changing intracranial environment.

TABLE 2.
Guidelines for the referral of head-injured patients to a neurosurgical centre

Indications for urgent referral to a neurosurgeon	CT scan shows a recent intracranial haemorrhage and/or haematoma
	Patient fits criteria for CT scan but scan cannot be performed locally
	Patient has concerning clinical features (see below) irrespective of CT findings
Clinical features which should be discussed with a neurosurgeon	Persisting coma (GCS score ≤ 8/15) after resuscitation
	Confusion that persists for more than 4 hours
	Deterioration in level of consciousness after admission
	Progressive focal neurological signs
	A seizure without full recovery
	Depressed skull fracture
	Definite or suspected penetrating injury
	A CSF leak or other sign of a basal skull fracture

CT = computed tomography; GCS = Glasgow Coma Scale

Although the use of ICP monitoring is not supported by class 1 evidence, the apparent relationship between ICP and outcome has resulted in the recommendation of ICP monitoring by consensus guidelines (Maas et al, 1997; Brain Trauma Foundation, American Association of Neurological Surgeons, Joint Section on Neurotrauma and Critical Care, 2000). ICP should therefore be monitored in all patients with severe TBI with an initial abnormal CT scan, and is most frequently carried out using a microtransducer or fibre optic probe inserted into the brain parenchyma via a burr hole. Alternatively, an ICP monitor can be placed in a lateral ventricle via an external ventricular drain and this also allows removal of CSF to reduce raised ICP. ICP monitoring allows calculation of CPP and detection of abnormal ICP waveforms. CPP is estimated by calculating the difference between MAP and ICP.

Transcranial Doppler ultrasonography of blood flow velocity in the middle cerebral artery provides an indirect assessment of CBF and can also be used to provide a non-invasive assessment of CPP. Transcranial Doppler ultrasonography is also useful in demonstrating pressure autoregulation and carbon dioxide reactivity in cerebral vasculature and the presence of cerebral vasospasm.

Jugular venous bulb oximetry is used to assess the balance between cerebral oxygen supply and demand. A catheter placed in the jugular bulb and dilatation of the internal jugular vein allows sampling of venous blood draining from the brain. Oxygen saturation can be measured from intermittent samples via the catheter or continuously using a fibre optic catheter. A reduction in jugular venous oxygen saturation, or an increase in the arteriojugular differences in oxygen content, indicates inadequate cerebral oxygen delivery and increased oxygen extraction ratio.

Treatment

Consensus guidelines for all stages of the management of patients after TBI have been issued (Brain Trauma Foundation, 1996; Maas et al, 1997) and are summarized in *Table 3*.

Ventilation: Controlled ventilation combined with adequate sedation is mandatory to maintain arterial blood gas targets. Hypoxaemia is present in up to 65% of patients with TBI because of factors such as direct pulmonary injury, aspiration of gastric contents, or neurogenic pulmonary oedema. High inspired oxygen concentration and the use of positive end expiratory pressure may be necessary to maintain adequate arterial oxygenation; however, positive end expiratory pressure >10 cmH_2O may impair venous drainage and lead to a secondary increase in ICP. Consensus guidelines recommend that $PaCO_2$ should be maintained between 4.0 and 4.5 kPa to maintain CBF, although many units now use $PaCO_2$ targets of 4.5–5.0 kPa for 'blind' therapy because of the risk of hypocapnic-induced cerebral vasoconstriction.

Cardiovascular support: Hypotension (MAP <90 mmHg) is associated with adverse neurological outcome and should be avoided (Chesnut,

TABLE 3.
Intensive care management of patients with severe head injury

Ventilatory parameters	Adjust ventilation to maintain PaO_2 >13 kPa and $PaCO_2$ 4.0–4.5 Pa
Haemodynamic parameters	Mean arterial pressure >90 mmHg
	Normovolaemia
Management of ICP and CPP	Treat ICP elevations above 20 mmHg
	Maintain CPP 60–70 mmHg
Accepted methods of management of ICP and CPP	Sedation
	Analgesia
	Mild to moderate hyperventilation
	Volume expansion plus inotrope or vasopressor when mean arterial pressure is insufficient to maintain CPP
	Osmotic therapy (mannitol)
If these methods fail to control ICP	More intensive hyperventilation ($PaCO_2$ <4.0 kPa)
	Therapeutic hypothermia (considered to be experimental at present)
	CSF drainage
	Decompressive craniectomy

CPP = cerebral perfusion pressure; ICP = intracranial pressure; MAP = mean arterial pressure; $PaCO_2$ = arterial carbon dioxide tension; PaO_2 = arterial oxygen tension. Modified from Maas et al (1997)

1997). A higher MAP may be necessary to maintain an adequate CPP in the presence of raised ICP. This should be achieved by fluid resuscitation to normovolaemia and administration of a vasopressor as necessary.

There is probably no 'best' fluid for patients with severe TBI although crystalloid and colloid are suitable (Zornow and Prough, 1995). Isotonic crystalloids are widely used and 0.9% saline is a scientifically justified choice. Glucose-containing solutions should be avoided because the free water liberated following the metabolism of glucose can worsen cerebral oedema. Additionally, in the anaerobic brain, glucose is metabolized to lactate, which worsens secondary injury.

Hyperglycaemia is associated with poor outcome following severe TBI and blood sugar should be maintained within a tight normal range (Lam et al, 1991). There has been interest in the use of hypertonic saline to facilitate low volume fluid resuscitation and this is associated with reduced ICP after TBI.

Sedation and analgesia: Sedation is an essential part of the management of severe TBI. Barbiturates were previously the mainstay of treatment; however, propofol is now the drug of choice because its favourable pharmacological profile allows easy titration of sedation levels and rapid wake-up. Propofol causes a dose-dependent reduction in cerebral metabolism, CBF and ICP while maintaining pressure autoregulation and carbon dioxide reactivity. Barbiturates still have a place in selected patients for the management of refractory intracranial hypertension.

Neuromuscular-blocking drugs have no direct effect on ICP but may prevent rises caused by coughing or straining on an endotracheal tube. Their routine use should be discouraged in favour of appropriate sedation with propofol, benzodiazepines (usually midazolam) and analgesia with opioids (such as fentanyl or morphine).

ICP and CPP control: Conventional approaches to the management of severe TBI have focused on the reduction of ICP in order to prevent secondary brain injury. Although it has not been demonstrated in controlled randomized studies that lowering ICP improves outcome, an ICP >20 mmHg is a powerful predictor of poor outcome after TBI and treatment should be initiated if ICP rises to >20 mmHg (Lang and Chesnut, 1995).

Over the last decade there has been a shift of emphasis from primary control of ICP to a multifaceted approach of maintenance of CPP, and the importance of maintaining cerebral perfusion and oxygenation throughout the entire management period is now accepted. There is general agreement that CPP should be maintained at >60 mmHg (Robertson, 2001; Brain Trauma Foundation, 2003) by control of MAP and treatment of intracranial hypertension.

Aggressive fluid replacement and cardiovascular support with vasopressors and inotropes effectively increases MAP and reduces the incidence of secondary cerebral ischaemia; however, this is associated with a high incidence of systemic (particularly respiratory) complications (Robertson et al, 1999). The risk:benefit ratio of ICP- or CPP-directed strategies should be assessed by appropriate monitoring techniques and therapy tailored to each patient individually.

Hyperventilation: Hyperventilation was once the cornerstone of ICP control after TBI. A reduction in $PaCO_2$ causes cerebral vasoconstriction and a fall in CBF, cerebral blood volume and ICP. However, hyperventilation only has short-lived effects on ICP, and empirical and excessive hyperventilation is associated with adverse neurological outcome (Muizelaar et al, 1991). Hyperventilation to $PaCO_2$ levels below 4.5 kPa may be required to control severe intractable intracranial hypertension in patients in whom carbon dioxide reactivity is maintained; however, this should only be undertaken in conjunction with jugular venous oxygen saturation monitoring to ensure that hyperventilation itself does not precipitate cerebral ischaemia.

Osmotic therapy: Mannitol, an osmotic diuretic, causes a reduction in brain volume and may be used to lower ICP after TBI. A Cochrane review concluded that mannitol was beneficial in the preoperative management of patients with acute intracranial haematomas; however, there is little evidence to justify its empirical and regular use in patients suffering raised ICP as a result of diffuse brain swelling (Roberts et al, 2003). Under certain circumstances mannitol can cross the blood–brain barrier and cause a reverse osmotic shift, leading to a rise in ICP. Hypertonic saline solutions also have a place in osmotherapy after TBI.

Therapeutic hypothermia: Modest reductions in brain temperature reduce the release of excitatory amino acids, and moderate hypothermia (32–34°C) has been shown to ameliorate axonal damage in animal models. However, a prospective, randomized study of moderate hypothermia in TBI was terminated early because of increased morbidity in patients over 45 years of age treated with hypothermia (Clifton et al, 2001). In this study,

however, patients who were hypothermic on arrival in the A&E department did better overall, and it has been suggested that active warming of patients who present with spontaneous hypothermia may be detrimental to outcome after TBI.

Notwithstanding these observations, moderate hypothermia remains a treatment option in many neurocritical care units because it is an effective means of reducing ICP. Pyrexia should be avoided at all stages of management because elevations in temperature worsen outcome after TBI.

CSF drainage: Drainage of CSF via an external ventricular drain is an effective means of reducing ICP. Although this is a widely used technique, there are no clear guidelines for its use. External ventricular drain insertion can be complicated by serious problems including infection, haemorrhage and seizures.

Decompression craniectomy: Removal of a bone flap with enlargement of the dura (duraplasty) is another therapeutic option for raised ICP refractory to conventional therapy. Although there is no definitive evidence that decompressive craniectomy improves outcome in unselected patients, it does favourably affect factors known to be predictors of poor outcome, such as raised ICP, brain tissue oxygen tension and basal cistern compression. Further investigation is clearly needed to identify the indications for decompressive craniectomy (Hutchinson and Kirkpatrick, 2004).

Miscellaneous: Nutrition is important in patients with TBI and early enteral feeding is associated with improved outcome. Feeding should begin as soon as possible following injury; many units aim to establish enteral feeding within 6–12 hours after admission.

Careful positioning of the patient is essential and elevation of the head reduces ICP while rotation of the head and flexion of the neck increase it. A neutral position of the head and neck with moderate head-up tilt (15–20°) is the optimal position after TBI; however, care must be taken to ensure that the head-up position does not cause a reduction in MAP and compromise CPP.

Seizures may occur after severe TBI, although their incidence is often overestimated. They are a potent cause of secondary brain injury, can be life-threatening and should be treated aggressively. Prophylactic anticonvulsant therapy is not practised widely in Europe, except for specific indications when phenytoin is a logical choice.

FUTURE ADVANCES IN NEUROSURGICAL INTENSIVE CARE

Miniature devices are now available to monitor brain tissue oxygen tension, which has been related to changes in CBF and low values correlated with poor outcome. Cerebral microdialysis is now possible at the bedside, and modern analysers are able to measure glucose, lactate, pyruvate, glutamate and glycerol levels in brain extracellular fluid. The lactate:pyruvate ratio gives information about the redox state of neurones, glutamate concentration is related to the degree of ischaemia, and increased glycerol concentrations (released from cell membranes) indicate neuronal death. Although cerebral microdialysis is presently a research tool, there is much interest in its use as a monitor to predict and measure cerebral ischaemia and identify potential windows for targeted neuroprotection.

Near infrared spectroscopy exploits the relative transparency of biological tissue to light, is able to measure changes in the concentration of cerebral oxygenated and deoxygenated haemoglobin, and has been used as a trend monitor of cerebral haemodynamics and oxygenation. Advances in technology have allowed the introduction of instrumentation that can make absolute measurements of cerebral oxygen saturation. Near infrared spectroscopy is a non-invasive, real-time technique that is also able to make simultaneous measurements from different areas of the brain, but significant technical issues must be resolved before it can be introduced into routine clinical practice.

A meta-analysis review of the use of corticosteroids in head-injured patients concluded that their use resulted in neither benefit nor harm (Alderson and Roberts, 1997). A large randomized controlled trial of the use of glucocorticoids after TBI, CRASH (Corticosteroid Randomization After Significant Head injury), is now underway. The trial aims to randomize 2000 patients with impaired consciousness after TBI to 48 hours of treatment with intravenous corticosteroid or placebo.

OUTCOME

Outcome after TBI depends upon the patient's age, GCS score on admission, and pupil size and reaction. Mortality and long-term outcome can be significantly improved by aggressive treatment in the first few hours after injury, although morbidity after head injury remains high, with around 50% of surviving patients having some form of residual disability at 1 year. This ranges from significant neurological disability to problems such as memory loss and difficulty with concentration. Early rehabilitation plays a crucial part in the management of the head-injured patient.

CONCLUSIONS

The management of patients with severe TBI requires an understanding of the underlying pathological processes and a coordinated, comprehensive and multidisciplinary approach to treatment. Prevention of secondary brain injury by avoidance of both hypotension and hypoxaemia is crucial to management. Pharmacological neuroprotective agents are unlikely to be available in the near future; however, effective resuscitation in the A&E department, and intensive care strategies to optimize cerebral perfusion and oxygenation, minimize the risk of secondary injury and maximize the potential for good neurological recovery. International consensus guidelines assist clinicians in providing the highest quality of care within the existing knowledge base, but these should not prevent the delivery of individually tailored therapy. HM

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KEY POINTS

- Neurological outcome following severe traumatic brain injury may be improved by prompt diagnosis appropriate early management.
- Avoidance of hypoxaemia and hypotension are crucial to the prevention of poor neurological outcome.
- Referral and transfer of the head-injured patient to a neurosurgical centre needs to be carried out promptly and safely.
- Definitive surgical treatment should only be delayed for life-threatening extracranial injuries.
- Intensive care management should comprise individually tailored strategies according to current best practice.

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