

# Secondary Brain Injury: Prevention and Intensive Care Management

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**Abstract:** Head Injury is one of the commonest causes of death. Most are the result of road traffic accidents. Primary Brain injury is the damage sustained as a direct result of the impact on the skull and intracranial contents. Secondary brain injury refers to the changes that evolve over a period of time (from hours to days) after the primary brain injury. It includes an entire cascade of cellular, chemical, tissue, or blood vessel changes in the brain that contribute to further destruction of brain tissue<sup>1</sup>. The purpose of this article is to outline the importance in early diagnosis and aggressive treatment of secondary brain injury so that further damage to brain can be prevented.

**Keywords:** Brain injury, secondary Brain Injury, Intensive care.

## INTRODUCTION

With rapid urbanization and mechanization, head injuries are assuming epidemic proportions. More often than not, outcome is marred by residual disability, which varies to a large extent from persistently vegetative, to subtle personality disorders. Besides the severity of primary brain injury, secondary brain injury is an important determinant of outcome. Most are the result of road traffic accidents, and the wastage of human potential is enormous.

## THE NATURE OF HEAD INJURY

Primary brain injury is the damage sustained as a direct result of the impact on the skull and intracranial contents. However, the neurological damage and associated vascular damage may trigger a sequence of events that lead to cerebral edema, cerebral ischemia and death or a persistent vegetative state. This cascade of events can be described as a secondary injury.

Whilst the primary injury in the brain can be fatal or give rise to severe disability due to neuronal destruction. A large number will subsequently deteriorate owing to cerebral ischemia from brain swelling, hematoma formation<sup>2</sup>, hypoxia and hypotension<sup>3,4</sup>. These are the main causes of secondary brain injury, which can be divided into intra – and extra cranial causes.

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## Intracranial Secondary Injury

### 1. Neurotoxic cascades

The danger of secondary injury is the result of the liberation of chemicals that cause disruption of the blood – brain barrier, edema and neural death either from direct trauma and ischemia or following the restoration of blood flow, the reperfusion injury<sup>5,6</sup>. The three most likely mechanisms of damage are the liberation of excitatory amino acids, platelet-activating factor and oxygen free radicals<sup>7</sup> with the ubiquitous nitric oxide radical just coming into the picture.

### 2. Calcium channel disturbance

It is believed that local tissue damage releases excitatory amino acids (EAAs), which in turn stimulate, for instance, N-methyl-D-aspartate (NMDA) glutamate receptors of calcium channels in the surrounding cells. There then follows a massive influx of calcium ions into the cells which leads to metabolic failure of the cells and cellular edema. Antagonists to NMDA glutamate or blockers of the NMDA glutamate receptor such as dizocilpine (MK-801) have been successful in preventing brain injury in animals<sup>8</sup>. Similarly voltage – operated calcium channel blockers such as nimodipine have also been shown to have some brain protective effects. Ketamine is an NMDA receptor antagonist that has been shown to improve neurological outcome in a rat brain injury model, but whether this will have practical value in a clinical setting remains to be seen. Cellular metabolic failure is associated with the generation of free radicals of oxygen. It is also associated with the release of platelet – activating factor from damaged cells and blood vessels.

### 3. Oxygen free radical production

Oxygen free radicals can be generated from several sources. The metabolic failure of cells generates free radicals. Ischemia and vascular damage can stimulate the arachidonic acid cascade, leading to prostaglandin and prostacyclin release and also leukotrienes with free radical generation. Platelet – activating factor may play an important role in free radical generation and the destruction of super oxide dismutase<sup>9</sup>.

Nitric oxide may also be important in the production of free radicals and by blocking nitric oxide synthase, outcome is improved. Experimental evidences suggest that antagonists to platelet – activating factor and leucocytes antibody treatment may also limit secondary brain injury<sup>10</sup>.

The free radicals also cause further vascular damage, again leading to an increase in vascular permeability and vasogenic oedema. This eventually leads to further brain swelling raised intracranial pressure, a decrease in cerebral perfusion pressure and more global ischaemia.

### 4. Hematoma formation

A skull fracture is frequently accompanied by rupture of a meningeal vessel. Such a bleed gives rise to an extradural hematoma which forms between the inner, bony table of the skull and the dura. This hematoma will compress the brain and cause local ischemia, a shift of midline structures and possible fatal brainstem damage<sup>11</sup>.

Subdural or subarachnoid hemorrhage is the result of traumatic rupture of cerebral vessels, causing a hematoma within the brain substance or in the space between the brain surface and the dura. The problem with subdural and subarachnoid hemotoma is that not only can they cause local compression and swelling of the brain substance and an increase in intracranial pressure, but also blood in the subarachnoid space can cause vasospasm and further cerebral ischemia.

### Extracranial secondary injury

#### 1. Respiratory failure

Loss of consciousness following head injury may be accompanied by a period of central apnea and can lead to severe hypoxia. Aspiration of vomit can cause further injury to lungs impairing ventilation. Any hypoxia will aggravate cerebral ischemia and increases cerebral blood flow and cerebral blood volume, thus increasing intracranial pressure. Thus any degree of respiratory failure is particularly hazardous for the patient with head injury.

#### 2. Blood Loss

Cerebral perfusion is partly determined by the cerebral

perfusion pressure (CPP), which is the difference between mean arterial pressure (MAP) and intracranial pressure (ICP)<sup>12</sup>. In a situation in which the ICP is raised, a fall in MAP may produce cerebral ischaemia. Hypotension from blood loss is not uncommon in multiple injuries and should be strenuously avoided and corrected. Blood loss can lead to anemia and make cerebral ischemia more likely.

### Other causes of secondary Injury

#### 1. Infection and Seizure

A major source of concern in open fractures of the skull is infection. Any patient with a cerebrospinal fluid (CSF) leak or who has air in the intracranial cavity and has an open fracture of the skull and should be given an appropriate prophylactic antibiotic regimen.

#### 2. Epileptic seizures

Early epilepsy is most likely to be associated with intracranial haematoma and depressed skull fracture. Sixty per cent of epileptic fits occur in the first 24 hours and about 10 per cent lead to status epilepticus. If the seizures are not controlled, they can cause cerebral hypoxia, which increases the secondary injury already present.

### MANAGEMENT

The sooner the medical treatment is available at the scene of an accident the greater is the chance of survival from head injury. One must first assess the airway and ensure a clear airway with adequate ventilation. Oxygen should be administered to any patient who is unconscious. Hypotension should be corrected by whatever means appropriate.

#### Loss of consciousness

A history of even a momentary loss of consciousness indicates a significant head injury. The duration of loss of consciousness probably relates to the severity of the primary injury. Continued loss of consciousness is most likely to be the result of diffuse brain injury. Focal signs of weakness or paralysis indicate focal brain damage but must be distinguished from immobility due to injury and pain.

#### Impaired consciousness

The Glasgow Coma Scale (GCS) in fact assesses impaired consciousness, coma being a severe degree of such impairment. The GCS scores the best eye opening, verbal and motor responses, and can be particularly useful in assessing whether a patient is improving or deteriorating neurologically. The motor responses in each of the four limbs should be recorded as well as the size and reaction of the pupils.

There should be a careful examination of the body for evidence of other injury in any patient with a head injury.

The advent of CT scanning has made a major difference to the diagnosis and early treatment of intracranial haematoma and a reduction in morbidity and mortality

### **Head – injured may be divided into three groups**

1. Those who are fully alert and oriented on arrival at the A&E department with or without a history of altered consciousness (GCS = 15)
2. Those with impaired consciousness (GCS = 8-14)
3. Those in coma or with deteriorating consciousness (GCS = 3-7)

It is well established that the outcome of head injuries with hematoma is a function of the time between the injury and the evacuation of the hematoma; therefore, transfer should not be delayed unnecessarily and care to be taken to avoid hypoxia and hypotension during transfer and also ensure sufficient monitoring in transfer.

### **Anesthetic Management**

The approach to anesthesia in head injury, although similar to that of elective neurosurgical procedures, can differ in many respects:

1. The presence of a full stomach.
2. Associated neck injury and facial injury with a potentially difficult intubation.
3. Extracranial injury, shock, anemia, aspiration, chest injury, and the need for resuscitation.
4. Evidence of raised ICP.
5. Likely postoperative intensive care management.

### **Induction and intubation**

In the acute head injury, there is seldom an indication for premedication. It might be best to regard all accident victims as having a potential full stomach. A rapid sequence induction would therefore be appropriate in the majority of cases.

### **Maintenance**

Once the airway and ventilation are secured, a longer acting muscle relaxant can be given without necessarily waiting for the depolarizing muscle relaxant to wear off. It is more important to prevent coughing and staining. If needed, analgesics may then be provided by potent short acting intravenous narcotics such as fentanyl and alfentanil.

Anesthesia can then be maintained with intravenous

thiopentone or propofol or with a volatile agent<sup>13</sup>. Isoflurane is probably the volatile agent of choice, as it appears to have least effect on the cerebral vasculature<sup>14</sup>. Ventilation should be controlled to keep PaCO<sub>2</sub> slightly below normal (4.5-4.0 kPa or 34-30 mmHg). Excessive hyperventilation is best avoided if ICP is raised, as it hampers the cerebral perfusion<sup>15</sup>. Hypotension should be corrected and fluids should be given to maintain a reasonable perfusion pressure<sup>16</sup>.

Postoperatively these patients will be cared for in an intensive care unit and sometimes electively ventilated and sedated for a period so as to stabilize their condition, to allow any swelling of the brain to subside and to reduce the chances of further bleeding.

The control of ICP is based on methods of altering the volume of the three major components of the intracranial contents, namely brain bulk, CSF and blood.

### **Alternations in brain bulk: Surgical Decompression**

A significant hematoma can be aspirated through a limited craniotomy. Severely contused brain tissue should be surgically removed as it is probable that the tissue would not survive to serve any useful function.

### **Reduction of cerebral edema: Diuresis**

Mannitol(20%) is probably the main osmotic diuretic used to reduce ICP. It is an osmotic diuretic and is given as a bolus infusion of 0.25-1.0 gm/kg<sup>16</sup>. Mannitol shifts water from the interstitial and intracellular compartments into the intravascular compartment, increasing the circulating blood volume and lowering blood viscosity. Although this may transiently increase cerebral blood flow (CBF) and cerebral blood volume (CBV), over all the effect is a reduction in ICP within minutes.

Several other hypertonic solutions have been used to promote a diuresis. Hypertonic sodium lactate and hypertonic saline/dextran 70 have been proposed as possible useful agents for reducing secondary brain injury<sup>17,18</sup>.

Furosemide (furosemide), a loop diuretic, will also cause some dehydration of brain tissue, and benefit ICP by mildly reducing CSF formation and encouraging CSF absorption. In combination with mannitol, it produces a marked diuresis which can lead to sodium depletion, unwelcome dehydration and pre-renal failure.

### **Fluid restriction**

In the case of acute head injury, when fluid loss due to injury is a problem and hypovolemic hypotension is a major

cause of cerebral ischemia, fluid restriction is not a good strategy and care must be taken to maintain intravascular fluid volume.

### **Steroids**

Although steroids can be useful in reducing edema that occurs around various intracranial tumors, they have not been found to be effective in reducing the edema of acute trauma and therefore are not used for this purpose after head injuries<sup>19</sup>.

### **Methods of altering CSF volume**

Hypertonic solutions, frusemide and acetazolamide reduce CSF production but probably not enough to be clinically important.

CSF is drained from the intracranial compartment by two mechanisms. First, CSF passes into the venous sinuses in the skull by a filtration-like process. This can be achieved by nursing the patient in the head-up posture and decreasing the hydrostatic pressure in the venous sinuses. Fluid restriction or venodilatation to reduce the venous pressure in the venous sinuses is inappropriate. It is also important to prevent a rise in venous pressure in the head due to obstruction of the jugular vein by tight clothing or excessive flexion or rotation of the neck.

Second, CSF can also pass out of the intracranial compartment into the spinal compartment through the foramen magnum. Gravity will assist the drainage of CSF into the spinal canal if the patient is positioned head up. Further rise in CSF pressure causing raised ICP can be managed with CSF drainage through intraventricular catheter so as to avoid herniation of brain matter.

### **Methods of altering intracranial blood volume**

Intracranial blood volume is quite small (60-80 ml), but in the condition of raised ICP, when the patient is on the steep part of the compliance curve, even small changes in the intracranial blood volume can have dramatic effects on ICP<sup>20</sup>.

The relations between cerebral blood flow, cerebral blood volume, cerebral vascular resistance, intracranial compliance and intracranial pressure are complex and not fully understood. They are influenced by the presence or absence of cerebral autoregulation. Because autoregulation is not necessarily uniform throughout the brain substance, the correct management in any particular circumstance is difficult to define, as one strategy that may benefit one part of the brain may not be appropriate for another.

### **Systemic blood pressure and autoregulation**

Cerebral blood flow is a function of the cerebral perfusion

pressure and cerebral vascular resistance. In normal brain there is an intrinsic autoregulatory mechanism which maintains cerebral blood flow. Autoregulation has a normal lower limit of 50-80 mmHg and upper limit of 130-170 mmHg mean arterial pressure, and the range is shifted upwards in hypertensive patients.

Hypotension is always detrimental because vasodilatation and a rise in ICP occur if autoregulation is intact, whereas decreased CBF with the danger of cerebral ischaemia occur if autoregulation is defective.

### **Cerebral venous blood volume**

About two-thirds of the cerebral blood volume is held in the venous capillary bed. Venous pressure significantly affects cerebral blood volume. Posture, coughing and straining, jugular venous and airway abstraction, positive pressure ventilation and many other factors that affect central venous pressure will alter cerebral blood volume. In a similar manner to CSF drainage, head-up tilt and careful positioning of the head will reduce ICP<sup>20</sup> and will be beneficial provided CPP is maintained<sup>21</sup>.

### **Volatile anesthetic agents**

In acute head injury it might be best to avoid such agents, although isoflurane is the least problematical provided ventilation is controlled<sup>14</sup>.

### **Hyperventilation**

It has been established that over the clinical range of arterial carbon dioxide there is a direct linear relation with cerebral blood flow. PaCO<sub>2</sub> and pH directly affect cerebrovascular resistance. Therefore, it is essential to avoid hypercapnia in patients with head injury as this will raise ICP<sup>15</sup>. Whilst hyperventilation is an effective way of managing acute intracranial hypertension, it should be remembered that it can produce a dangerous decrease in cerebral blood flow, especially if CPP is low.

### **Hypoxia**

Hypoxia increases cerebral blood flow and cerebral blood volume and increases intracranial pressure. Hypoxia should be strenuously avoided.

### **Cerebral Metabolic rate**

There is also a direct relation between cerebral metabolic rate, cerebral oxygen consumption and cerebral blood flow and volume. Any decrease in cerebral metabolic rate will decrease ICP.

Induced hypothermia was used as a technique for cerebral protection in neurosurgical anesthesia many years ago but, because the technique is complicated and troublesome, it is now seldom used. Hypothermia also preserves protein kinases which are otherwise destroyed

in normothermic ischemia<sup>22,23</sup>. These protein kinases limit intracellular calcium accumulation and protein phosphorylation. The time may be approaching when the role of induced hypothermia should be seriously reviewed<sup>24</sup>.

### Intravenous sedative and analgesics

Intravenous opioids and barbiturates decrease cerebral metabolic rate and lower ICP. At the same time they may cause a fall in blood pressure<sup>13</sup>. They should be used with controlled ventilation to prevent hypercapnia from respiratory depression<sup>15</sup>. Because barbiturates are known to be free radical scavengers, they were in vogue for deep barbiturate coma in the treatment of head injury<sup>13</sup>. Similar effects are evident with usage of propofol especially in lower doses.

The intensive care of head injured patient should be meticulous with special attention to skin, nutrition, and joint care besides maintaining cardiovascular, respiratory and fluid balance.

### Neurological observations and monitoring

The patient with a head injury who is being sedated and who has also been given analgesics and muscle relaxants cannot be accurately assessed neurologically. The Glasgow Coma Scale is meaningless and most reflex responses will be altered in some way. Probably the only reliable response is that of the pupil to light, which will continue to signify the integrity of the brainstem. Other forms of investigation are required. The two main methods are repeated CT scanning and ICP monitoring.

### CT Scanning

CT scanning is often regarded as being more important than ICP monitoring. Serial CT should be carried out in patients showing no recovery, neurological worsening or in whom neurological recovery has plateaued, for early detection of secondary brain injury. Moreover, effects of cerebral edema can be quantified on CT as a grade ranging from 1 to 4 depending on the severity.

### ICP measurements

ICP monitoring can offer the following:

1. Continuous display of ICP.
2. Accurate calculation of cerebral perfusion
3. Prognostic significance.
4. Assessment of intracranial compliance.

### Other forms of monitoring

**A-mode Doppler ultrasound** is a useful and sensitive method for detecting a shift in midline structures.

**Jugular venous PO<sub>2</sub>**. Can demonstrate cerebral hypoxia.

The combination of jugular venous saturation and lactate level may be more meaningful<sup>25</sup>.

**Visual evoked responses** or **somatosensory evoked responses** have been used for the assessment of brainstem damage.

**NIRS, TCD SPECT, CSF Chemical markers** are monitoring tools to prognosticate the outcome, but require confirmation.

### Outcome

The outcome following head injury can be defined crudely in terms of death and survival. The mortality in severe head injury (GCS<9) has fallen from about 50 per cent to 30-40 per cent in recent years. However, often it is the quality of survival that is more relevant. **Jennet and Bond** devised a scheme, the **Glasgow Outcome Scale**, which attempts to describe the overall social capability or dependence of the individual, using five main categories:

1. Death.
2. Vegetative state (absence of awareness).
3. Severely disable (conscious but disabled and dependent).
4. Moderately disabled (disabled but independent).
5. Good recovery (resumption of normal life.).

Categories 3-5 can be subdivided into further degrees of disability.

The Glasgow Outcome Scale is a practical scale to assess disability, which can be applied with consistency by a wide range of clinicians. Used in conjunction with the Glasgow Coma Scale, the Glasgow Outcome Scale can form the basis for the comparison and cost-benefit analysis of different regimens of treatment.

### Ethical Issues

The management of head injury often presents medical and nursing staff with difficult moral and ethical decisions. The majority of the difficult decisions are focused on the withholding or withdrawal of life-sustaining therapy.

A patient who fulfils the criteria for the diagnosis of brainstem death does not pose an ethical dilemma. The decision 'not to resuscitate' if a cardio-respiratory arrest occurs is also relatively easy decision which should be based on the likely outcome of the illness and the predicted quality of life.

The more difficult decisions are whether to embark on a course of investigation and treatment that is unlikely to benefit the patient or to withdraw treatment when it is considered 'futile'.

It is generally accepted that the use of critical care resources should be governed by four basic considerations: patient autonomy, beneficence, non-maleficence and justice.

The decision – making can be greatly helped by having guidelines for the admission to and discharge from the intensive care unit. These guidelines should be agreed to by the clinicians and nursing staff and approved by the hospital management and in particular their legal department.

## CONCLUSION

Managing head Injury is a challenging task and requires dedicated efforts and good team-work round the clock for better outcome.

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