Chapter 8: Cerebral protection

Stephen Lo

Introduction

There will be a variety of neurological pathologies that you will see within the intensive care. The purpose of this chapter is not to cover all neurological emergency, but rather general principles of cerebral protection. While the primary injury of the CNS is often untreatable, the aim in significant CNS insult is to minimize secondary injury. The primary insult can include a variety of pathology, but the main ones you will see within the ICU include traumatic brain injury (TBI), intracerebral haemorrhage, hypoxic brain injury (such as in cardiac arrest), cerebral infection, inflammation and cerebral embolic stroke.

Secondary injury

These are injuries that occur in viable brain tissue as a result of insults relating to the primary pathology. Commonly, this includes cerebral swelling and loss of autoregulation. This leads to cerebral hypoperfusion and hypoxia which leads to further injury.

Cerebral swelling

The primary insult causes areas of the brain to be injured and die. This leads to release of chemical mediators and inflammation. There is disruption of blood brain barrier and capillary leak causing swelling. The inflammation is similar to that which occurs at other tissue, except the key difference is that the cranium has a fixed volume. This means there is only a very small capacity for the brain to swell before the pressure in the cranium increases. There are three main components within the cranium: mass (brain + some mass, such as tumour), blood and cerebrospinal fluid (CSF). Initially an increase in cerebral swelling will cause a shift in CSF as well as venous cerebral blood, nullifying the pressure increase, but once this redistribution is exhausted, intracerebral pressure will build. As the pressure builds, the blood flow to the rest of the brain will be reduced. A simple formula to estimate blood flow is to look at the difference between the intracerebral pressure (1) and mean arterial pressure.

$$CPP = MAP - ICP$$

CPP=Cerebral perfusion pressure

MAP=Mean arterial pressure

ICP=intracerebral pressure

If jugular venous pressure (JVP) exceeds ICP, then JVP replaces ICP

$$CPP = MAP - JVP$$

This is a very crude equation to use, but it is the basis of ICU therapies for neurological pathologies. For reference, normal ICP is 5-15mmHg.

Loss of autoregulation

Normally the brain has the ability to control the cerebral blood flow according to changes in systemic blood pressure. In an injured brain, this is lost. Hence there is great focus on blood pressure management in neuroprotection.

Cerebral protection

There are numerous treatments that we employ to prevent secondary injury (2). Many of our therapy are based on the formula of CPP=MAP-ICP. The idea being, increasing MAP and decreasing ICP.

Blood pressure therapy

Blood pressure therapy. In general, a higher MAP means a higher cerebral perfusion pressure and therefore blood flow to the injured brain. A common target for MAP is aiming for cerebral perfusion pressure of 60mmHg. If a patient has an ICP monitor this can be calculated by the above formula. If the patient does not have one, then a MAP of 90mmHg is common used, as it assumes that the ICP is 30mmHg. The problems with hypertensive therapy are that in certain pathologies, they may increase bleeding and therefore ICP. Common example of this is intracerebral haemorrhage and subarachnoid haemorrhage with an unprotected aneurysm. In this instance, there is a balancing game at play, and an adjustment in the blood pressure target is required. An example of a MAP target is a lower limit of 70-80mmHg and an upper limit of 90-100mmHg.

Reducing intracerebral pressure

This is the cornerstones of cerebral protection. There are medical and surgical management to achieve this.

Medical management

There are four broad categories of reducing ICP (3). These are reducing swelling, reducing cerebral metabolic rate, reducing jugular venous pressure, and reducing excessive cerebral blood flow.

Reducing swelling

This is the use of drugs to reduce swelling of the brain. There are two main agents: osmotic agents and steroids.

Osmotic agents

Osmotic agents reduce swelling by decreasing intracellular water by increasing the osmolarity of the extracellular fluid. There are two agents that are used: Hypertonic saline and mannitol.

Mannitol

Mannitol is given at a stat dose of 0.5-1g/kg. It comes as 20% Mannitol (which means 200g/L) and hence a common dose is a 500ml bag of 20% mannitol. In the critically ill it is only given where there is unilateral pupillary dilation where impending coning has occurred on initial presentation (usually in ED). This buys sometime by temporarily dropping the ICP, hopefully enough time for a CT head or neurosurgical intervention to occur. This is usual in the initial presentation because it does not require central access to be delivered and does not have the acute hypotensive effect of hypertonic saline. It will eventually cause diuresis and subsequent hypotension. It drops the serum sodium and cannot be measured and is therefore not used in patients outside of the initial presentation.

Hypertonic saline

In the treatment of cerebral oedema (4), the dose given is 20ml of 4M NaCl (23% NaCl) over 30min. It is preferable to administer this through central access as it is highly corrosive, although in emergent situations, it can be slowly administered through a peripheral line (like most agents). Given too quickly, you may drop the BP. It is the preferred agent as it is easily measurable and monitored and has less of the diuretic effect of mannitol (5). Na targets can range from 145-160 in patients with cerebral oedema. This is the mainstay of osmotic therapy within the ICU.

Steroids

Steroids act by reducing inflammation and capillary leak to reduce cerebral swelling. It is used in cerebral swelling related to tumours and meningitis. It is not used in traumatic brain injury as studies have shown it to cause an increase in mortality.

Reducing cerebral metabolic rate

Reducing cerebral metabolic rate not only reduces the intracranial pressure by reducing the increasing blood flow that is required but also reduces the mismatch between supply and demand and therefore reduces cerebral ischaemia. A number of interventions can be done to reduce cerebral metabolic rate:

Sedation and anaesthetic agents

Most sedatives (6) used in ICU can achieve this: propofol and midazolam are the common agents that are used. In severe cases of cerebral oedema in TBI, sometimes a barbiturate is used e.g. phenobarbitone, thiopentone infusions. Barbiturates are potent agents which lower metabolic rate and reduce ICP, however, they have immunosuppressive effects and

take a long time to be cleared from the body. They are only used as third line agents for the treatment of a high ICP.

Detection and treatment of seizures and pain

These should be promptly treated. Pain should be treated with opioids. Remifentanil is a good agent to use, as it has a short half-life and can be easily turned off to assess neurology. Prophylactic antiepileptic is sometimes used in patients at risk, depending on the pathology.

Avoidance of hyperthermia

Hyperthermia increases cerebral metabolic rate and hypothermia does the reverse. In patients with TBI, there is a narrower temperature range that is acceptable. In refractory cerebral swelling, sometimes hypothermia is employed. Temperature is reduced by paracetamol or simple exposure methods, but often active cooling is required with cooling mats. If that occurs, patients may need muscle relaxants intermittently to avoid shivering, as this is uncomfortable for the patient and can increase ICP. Therapeutic hypothermia (7) can be also used for refractory high ICP, but this has potential complications and should be a consultant decision.

Reducing jugular venous pressure

The cerebral veins drains into the jugular veins. Hence an increase in pressure in the jugular pressure will be transmitted intracranially and raise the ICP. The jugular pressure can be reduced by placing the patient head up and avoiding obstruction and occlusion of the jugulars, such as with a neck collar. Check and adjust the collar such that there is no venous occlusion. Increase in airway pressure will also increase the jugular pressure and therefore care needs to be taken to avoid excessive airway pressure.

Minimizing excessive vasodilation

Arterial carbon dioxide and a low pH are potent vasodilators of the cerebral blood vessels. In ventilated patients, $PaCO_2$ is relatively easy to control by increasing the minute ventilation, and hence a low normal $PaCO_2$ is targeted (4.5-5.0). Hyperventilation ($PaCO_2$<4.5kpa) can be employed to immediately drop the ICP, but can cause excessive vasoconstriction causing ischaemia. Prolonged hypocarbia (8) causes a shift in the "setpoint" of pCO_2, meaning that the vasoconstrictive effect will decrease. Therefore, hyperventilation is only used as a temporary measure in emergency such that definitive therapy can be instituted. *For more info about ventilation, please refer to chapter 2 and 3 in respiratory failure and mechanical ventilation.*

Surgical interventions

There are variety of surgical interventions that are employed in the management of high ICP. These are decided between the neurosurgeons and the ICU consultant.

ICP monitor (bolt)

This can be done within the ICU. This is not an intervention as such, but is commonly used in patients with severe TBI to guide therapy (9).

Extra ventricular drain (EVD)

Insertion of a tube to the lateral ventricle to allow for the drainage of CSF, and reducing ICP. It can also be used to monitor the ICP. It is used in patients with hydrocephalus was well as patients with high ICP in traumatic brain injury which is refractory to medical management.

Evacuation of mass

In pathologies where there is mass effect, one potential management is surgical removal. This may include abscess drainage, tumour excision and clot evacuation. Removal of the mass will reduce ICP, but remember that swelling in the residual injured tissue may still occur causing a rebound high ICP, depending on what was done.

Decompressive craniectomy

This is the removal of the bone flap, allowing the brain to swell without increasing ICP. This is a controversial therapy. This is used in haemorrhage, cerebral stroke and TBI. There is no doubt that ICP control is better, but whether it improves mortality or most importantly disability in survivors, it is still not clear (10) (11) (12) (13). A decision on whether this should be done depends on the pathology, the patient and requires consultation with the consultant and neurosurgeon.

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