CURRENT CONTROVERSIES IN TRAUMATIC BRAIN INJURY

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This talk is not designed to be a replacement for a good neuroanaesthesia textbook, or in any way a comprehensive overview of the topic… it is too large to even try to cover in 20mins!

This talk is not going to cover pre-hospital care, ICU care (including biomarkers), neuro-monitoring, paediatrics, brain death / organ donation, or the long-term neurocongnitive effects of head injury.

However I hope that by the end of the talk I will have given you a brief outline of some of the areas in traumatic brain injury (TBI) that are of particular interest to anaesthetists; if you wish to follow any of this up further I have attached a fairly comprehensive and (I think) up-to-date reference list so that you can easily find the source material.

Introduction

TBI, which has been called the "silent global epidemic," is the leading cause of death of children in the developed world, a major killer of (particularly) young men in the developed world with enormous emotional, social and financial costs to society. Falls in the elderly (>75 years) are also increasingly represented.

Classification of TBI is based on the GCS with severe TBI defined as a GCS <9 for more than six hours. Mortality is closely related to the initial GCS (plus age and type of lesion).

The incidence estimates for TBI range from 100-200/100,000 population. In the USA 30,000 people / week suffer a TBI and 1000 / week will die, with costs of $US60B / year! TBI is now a major focus of US public health and law programmes.

The mortality rate has stuck at 30-35% since the 1980s while the mortality attributable to TBI for poly-trauma victims who reach hospital is approx 90%. There is now clear evidence that outcome from TBI is worse in "general" hospitals as compared to those with specialist neurosurgical and neuro-ICU units, that can't simply be explained by "good" neuro-triage (ie poor prognosis patients not being transferred to specialist care). The Australasian TBI Study (ATBIS) has looked at the epidemiology and outcome from TBI in Australia & NZ in a prospective six month study. They found that young men in high speed (>70km/h) MVAs predominated, and that in 25% of cases there was clear evidence of early secondary brain insult (specifically hypotension and hypoxia). Thirty-five percent of patients required an immediate operation.

Following a head injury there is an initial primary insult resulting from the biomechanical effect of forces applied to the skull and brain manifested in milliseconds. Although there is enormous heterogenicity in TBI, the common theme is the development of secondary injury occurring over minutes to days, as the result of the common mechanism of cerebral hypoxia with ischaemia setting up the "vicious cycle" of brain swelling and oedema. This is a mixture of cellular energy failure, inflammation activation and blood brain barrier leak, sometimes termed vasogenic & cytotoxic oedema. Because the cranial vault is a rigid structure (Monroe-Kelly doctrine), as oedema develops, ICP increases with limited ability for compensation (CSF or venous shunting and brain displacement / herniation). ICP / oedema is aggravated by systemic hypoxia, hypercarbia, hypotension, anaemia and hyperglycaemia. These contributing factors are generally preventable (or at least manageable) and form some of the basis for EBM guidelines for the management of TBI (eg Cochrane and Brain Trauma Foundation BTF) and represent some of the areas where management is controversial!

In fact there is very little level one EBM to support TBI management with no level one evidence to support the use of any monitoring modality, physiological threshold for treatment, ICP level or CPP optimisation!
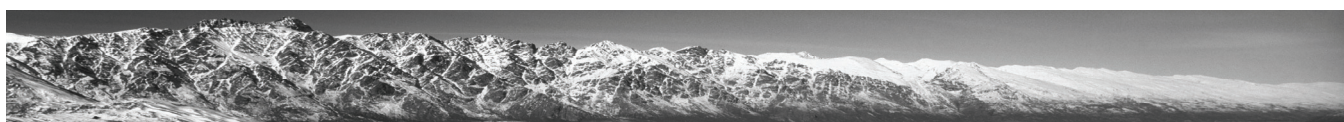
There may also be associated systemic complications or non-neurological organ dysfunction after TBI, particularly cardiac (as a result of massive catecholamine outflow / sympathetic over activity), acute lung injury / pneumonia and coagulation abnormalities.

Cervical Spine Clearance in Severe TBI Patients

Cervical spine injury occurs in 5-8% of severe TBI patients. There has been controversy about appropriate "clearance" of the cervical spine prior to removal of the hard collar. Passive flexion-extension x-ray studies with dynamic fluoroscopy (DF) do not add any information to that obtained by plain radiographs and fine-cut 1mm CT (C0-C3) and 3mm CT (C3-T2) plus reformatting.

Saline or Albumin for Fluid Resuscitation

While the SAFE study showed no significant difference in the risk of death in heterogeneous ICU patients resuscitated with either saline or albumin there was concern about a trend towards unfavourable outcome in those patients resuscitated with albumin who had TBI. Therefore a post-hoc analysis was done (SAFE-TBI study). Outcome measures were mortality and functional neurological outcome (GOS score) 24 months post-randomisation. At 24 months 33.2% of the TBI / albumin group had died compared to 20.4% in the TBI / saline group. In those with severe TBI the mortality was 41.8% and 22.2% respectively. Most of the mortality occurred in the first 28 days. For favourable GOS scores, the results were 47.3% (albumin) and 60.6% (saline).

Decompressive Craniectomy (DC)

While the need for neurosurgical evacuation of TBI-related hematoma is not (really) controversial, surgical management of diffuse brain injury with persistent swelling is. In the last 10 years there had been renewed enthusiasm for DC, with numerous anecdotal reports of favourable outcome.

The DECRA study randomised 155 adults in Australia, NZ & Saudi Arabia between 2002-2010, with severe diffuse TBI and intracranial hypertension refractory to "first-tier" therapy to either bifrontal DC and dural opening or continued "standard care." DC produced dramatic and obvious short-term improvements (decreased ICP, medical therapy, ventilation time and ICU stay) but eventual functional outcome measured at six months was the opposite.

There were 19% more patients with poor functional outcomes and 23% more survivors with severe disability in the DC group. The cause for this poorer outcome is unclear but there is speculation that axonal stretch as the brain swelled out of the cranial vault through the DC defect produced an unexpected "brain volu-trauma." Based on the results of DECRA, DC can't be recommended for treatment of severe TBI (without haematoma) with refractory intracranial hypertension. Cost savings in Australia alone from avoiding DC are estimated to be $A100m.

The RESCUEicp trial (yet to report) is addressing a similar question in the UK & Europe, albeit at higher threshold ICPs (25mmHg) for longer periods of time (1-12 hours).

ICP

ICP monitors should be placed for GCS <9 and abnormal CT (or two of – age > 40, SBP < 90, motor posturing). Management of elevated ICP (> 20mmHg) will generally follow a step-wise algorithm and is aimed at reducing "brain bulk" and supporting arterial pressure. All of the steps can be initiated in the operating theatre, although induction of hypothermia must be done with extreme caution and with an understanding of the potential pitfalls.

Generally CPP (MAP-ICP) should be maintained in the range of 50-70mmHg with adequate fluid resuscitation and vasopressors. CPP is a major determinant of CBF which, under ordinary circumstances with intact cerebral autoregulation, is relatively constant across a wide range of CPPs (typically 50-150mmHg). Outside these limits, or when cerebral autoregulation is lost, CBF becomes directly dependent on CPP. CPP should not be augmented if ICP < 20mmHg.

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Hyperventialtion

The cerebral vasculature is rapidly responsive to $PaCO_2$ even after TBI and therefore hyperventilation will cause decreased CBV and ICP. However the concurrent reduced CBF will increase the volume of critically hypoperfused brain tissue and therefore worsen brain ischaemia. In addition, the "benefit" of hypocapnia is short lived as cellular mechanisms compensate for the changes in CSF pH by 24 hours, with associated rebound ICP rises as CO_2 levels return to normal.

Acute hyperventilation should only be used as a "live saving" procedure for managing acute neurological deterioration until definitive imaging and neurosurgical intervention is undertaken.

Osmotherapy

Mannitol (0.5-1.5g/kg over 15-30mins) reduces ICP through a haemodynamic effect and an osmotic effect. The immediate plasma expanding effect of a bolus of mannitol alters blood rheology with reduced CVR and increased CBF. Autoregulatory vasoconstriction may then decrease CBV and ICP. There is then a delayed osmotic effect ("brain shrinkage") that develops over 30mins, although this direct removal of water from the brain parenchyma may contribute less to the fall in ICP than the initial haemodynamic effect.

Hypertonic saline (HTS) has similar immediate haemodynamic and delayed osmotic effects. The advantage of HTS is that it is less likely to cross the BBB causing delayed rebound cerebral oedema. It is also said to improve pulmonary gas exchange, decrease leucocyte adhesion and modulate the inflammatory response. Disadvantages are central pontine myelinosis, CHF, ARF, and hyperchloraemic acidosis.

Glucose Control

Hyperglycaemia (HG) (glucose > 7.8mmol/L) is attributed to the stress response following the initial TBI, and is associated with poorer outcomes. The severity of HG probably reflects the severity of TBI and places the brain at risk of secondary injury via glucose driven oxidative stress. The intraoperative period has been shown to be a time of particular risk and therefore a time for therapeutic intervention… ie insulin! The anaesthetic / surgical process can drive up blood glucose level as can steroids. The exact blood glucose at which to intervene is unclear, although if insulin therapy is started, it is critical to avoid hypoglycaemia.

Hypothermia

Mild hypothermia (32-35°C) induced in the first few hours after an ischaemic event can prevent or mitigate permanent neurological injury. Although the evidence is strongest for post-cardiac arrest global ischaemic encephalopathy and neonatal asphyxia, the ultimate mechanism of injury (ie ischaemia) is fundamentally the same as that in TBI. There are a multitude of mechanisms by which hypothermia is thought to provide its protective effects of which "reduced metabolism" is only one. There have been numerous studies of hypothermia in TBI, without clear evidence of beneficial outcome, although the studies have been plagued by methodology and implementation issues, in particular controlling the known and expected side effects of cooling (eg CVS effects, coagulation, glucose control).

Cooling is effective in patients with severe TBI and raised ICP as long as it is initiated early, continued for 2-5 days, patients are re-warmed slowly and side effects are properly managed.

The POLAR trial is currently being conducted to look at the effects of early "prophylactic" cooling (33°C) for 3 days in TBI to answer this question with more certainty.

Fever, irrespective of cause, can adversely affect neurological outcome and must be controlled.

Pain Management

Studies have shown that significant numbers of patients have severe post-craniotomy pain.
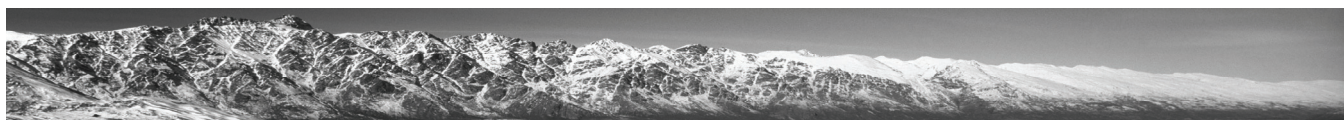
A number of pain management strategies have been published recently. Intravenous paracetamol has been shown to increase patient satisfaction with pain relief following spinal surgery, without reducing the morphine requirement. Use of a COX-2 inhibitor (rofecoxib) in conjunction with narcotic analgesia has been shown to reduce pain, length of stay and hospitalisation costs. Local anaesthesia scalp blocks have also been shown to be an effective means of providing transitional analgesia with a duration of effect that far outlasts the pharmacology of the local anaesthetic.

The use of PCAs are now well established in neurosurgery with studies of PCA morphine or fentanyl showing better analgesia, less vomiting and greater satisfaction levels compared to conventional IM / IV bolus regimes, without any differences in sedation or CO_2 levels.

Proper management of post-craniotomy pain has been the subject of a recent editorial in Anesthesia and Analgesia where Allan Gottschalk stated, *"PCA now seems effective after craniotomy…"* and… *"the development of multimodal analgesia strategies that maximize analgesia while limiting the dose of any one drug so as to reduce or eliminate meaningful side-effects such as sedation and respiratory depression seem to be particularly desirous for patients undergoing intracranial surgery."*

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