Traumatic Brain Injury Part III:

Assessment and Management of

Severe TBI

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First Edition Update 2022

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Intended Learning Outcomes

TBI Part III: Assessment and Management of Severe TBI

1. Identify the most important aspect in the assessment of severe patients with TBI
2. Explain the role of ICP monitoring in patients with TBI
3. Describe further monitoring techniques for TBI patients
4. Describe therapeutic interventions in TBI patients and list the criteria for specific interventions such as surgery
5. Discuss basic and second line interventions in brain oedema in patients with TBI
6. Describe the diagnosis and management of intracranial infections in patients with TBI
7. Describe the diagnosis and management of seizures in patients with TBI

eModule Information

Relevant Competencies from CoBaTrICE

TBI Part III: Assessment and Management of Severe TBI
• **2.2** Undertakes timely and appropriate investigations • **2.8** Liaises with radiologists to organise and interpret clinical imaging • **2.9** Monitors and responds to trends in physiological variables • **2.10** Integrates clinical findings with laboratory investigations to form a differential diagnosis • **3.6** Recognises and manages the patient with neurological impairment • **4.4** Uses fluids and vasoactive / inotropic drugs to support the circulation • **6.3** Manages the care of the patient following craniotomy under supervision

1. Assessment Of Severe Brain Injury

The Glasgow Coma Scale (GCS), a clinical scoring system designed to assess coma, impaired consciousness, and motor responses, is one of the most commonly used to communicate severity of injury (it should be scored after basic resuscitation). Patients with GCS scores of 3 to 8 are classified as ***severe*** TBI, those with scores of 9 to 12 are classified as ***moderate*** TBI, and those with scores of 13 to 15 are classified as ***mild*** TBI. Patients with severe TBI require intensive care admission either to a surgical-trauma ICU or a neuro-ICU depending on associated injuries and/or local hospital organisation and resources. Patients with moderate injury may also require close monitoring and an ICU setting for a decline in neurological status and/or airway compromise and/or to monitor ICP if there is a risk of evolution of a mass lesion.

1. 1. Neurological monitoring

Some measurements are considered routine in specialised centres and units. Others are more experimental, more complex and their value in the management of individual patients still uncertain.

Standard measurements

- Neurological status (GCS, brain-stem reflexes, motor exam)
- ICP/CPP

Advanced measurements

- Brain tissue PO2 ($PbtO_2$)
- Pressure Reactivity Index (PRx)
- Thermo-dilution CBF
- Jugular bulb oximetry ($SjvO_2$)
- Transcranial Doppler flow velocities and pulsatility indices
- Evoked potentials
- Continuous surface EEG
- Cortical depth electrodes or subdural strip electrodes (Electrocorticography)
- Cerebral Microdialysis
- Near Infrared Spectroscopy (NIRS)

1. 2. ICP monitoring

A good grasp of three physiological concepts will aid your management of patients with TBI. To refresh:
Intracranial volume is a constant in adults. An increase in any of the component volumes (blood/CSF/brain/pathological mass) must result in a decrease in one or more of the others (Monro-Kellie doctrine).
The relationship between intracranial volume and pressure is represented by the pressure–volume curve. This curve has three zones: a flat zone, expressing good compensatory reserve, an exponential zone, depicting poor compensatory reserve, and a flat zone again, seen at very high ICP (above the ‘‘critical’’ ICP and associated with derangement of normal cerebrovascular responses). The pulse amplitude of ICP is low and does not depend on mean ICP in the first zone; it then increases linearly with mean ICP in the zone of poor compensatory reserve. In the third zone, the pulse amplitude starts to decrease with rising ICP.
Cerebral perfusion pressure (CPP) is defined as the difference between mean arterial pressure and mean ICP i.e. CPP = MABP – ICP (provided that sagittal sinus pressure does not exceed ICP).

Raised ICP occurs in approximately 50% of all patients with mass lesions and 30% of all patients with severe diffuse injuries. Uncontrolled, refractory ICP correlates strongly with mortality. Mortality and morbidity in patients with head injuries is directly related to the duration of ICP above a threshold of 20-25 mmHg. The relevance of continuous ICP monitoring is highlighted once a digital continuous recording is obtained. Continuous digital monitoring is more accurate than nurse led hourly episodic measurement of ICP.

In text References

(Andrews and Citerio. 2004; Citerio and Andrews. 2004; Czosnyka and Pickard. 2004)

1. 2. 1. Definitions and normal values

Intracranial pressure is defined as the cerebrospinal fluid pressure measured via a catheter in the ventricular system with its tip at the level of the Foramen of Monro - without loss of fluid from the system- (equivalent to ventricular fluid pressure, VFP).

Normal values of VFP:

- Newborn: <7.5 mmHg
- Child: <10.0 mmHg
- Adult: <15.0 mmHg

ICP can be recorded at various sites in the cranial vault. Fluid pressures can be recorded in the ventricular system, the cisterna magna, and parenchymal pressures in

the brain tissue itself at various locations (e.g. supra- or infra-tentorial). Pressures can also be recorded in the subdural, subarachnoid or epidural space. Subdural and epidural ICP recordings are not particularly reliable and are not recommended for monitoring.

Note

Different sites, different values

It must also be kept in mind that, especially in cases with mass lesions, ICP gradients may occur which are the driving force for brain-shift and herniation. This is particularly clinically relevant for temporal and frontal masses. In cases of compartmentalized mass effect, VFP may not reflect the risk of compartmental tissue shift and herniation.

Challenge

Why is intracranial volume constant? Given that the relationship between intracranial volume and pressure is exponential, construct a graph of the relationship.

Intracranial haematomas in the infratentorial space are much more dangerous, as this is a very small compartment compared with the supratentorial space (risk for direct, life-threatening brain stem compression).

Task

Test your knowledge

In which situation(s) does withdrawal of CSF via a ventricular catheter lower(s) ICP most?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

If overt hydrocephalus is present (rare in TBI) or a subtler disturbance of CSF reabsorption has occurred.

Even if no overt hydrocephalus is present, withdrawal of CSF may be beneficial if ICP is very high. Why?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Such a situation suggests operating on the exponential portion of the intracranial pressure/volume curve and the withdrawal of small volume induces a relatively large reduction of ICP.

Why, in the above circumstance, might the beneficial effect be unfortunately transient in nature?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Because accumulation of the cerebrospinal fluid was not the original cause of the elevated ICP, the effect in lowering ICP is transient. Also, with an expanding mass lesion CSF is driven towards the thecal sac and so CSF drainage tends to be of limited value.

1. 2. 2. Components of the basic ICP waveform

Under normal conditions cardiac and respiratory waves are superimposed on the baseline level of ICP, resulting in a characteristic waveform. It remains unclear whether the pulsatile fluctuations of ICP are primarily arterial, venous, or combined in origin. ICP values are also dependent on the intrathoracic pressure, which influences venous outflow from the intracranial space. In fully ventilated patients, inspiration increases ICP and expiration causes ICP to decrease (the effect of intrathoracic pressure and PEEP on ICP is contingent on both cranial and respiratory system compliances).

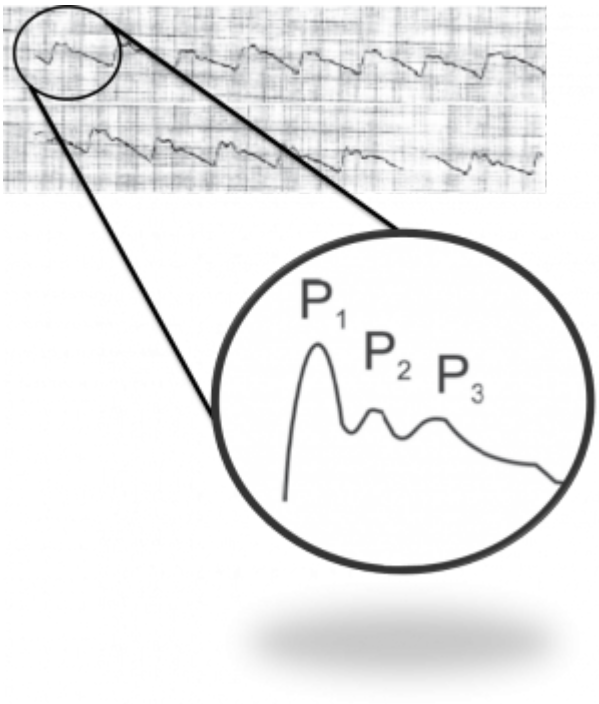

Figure 16: Cardiac components of the ICP wave: P1 (reflects arterial pulsation), P2 (reflects, to a degree, intracranial compliance) and P3 (reflects aortic valve closure)

Webcast:

Neuromonitoring, ICP curve interpretation, threshold and pitfalls

References

- Andrews PJ, Citerio G., Intracranial pressure. Part one: historical overview and basic concepts., 2004, PMID:15243684
- Citerio G, Andrews PJ., Intracranial pressure. Part two: Clinical applications and technology., 2004, PMID:15243685
- Czosnyka M, Pickard JD., Monitoring and interpretation of intracranial pressure., 2004, PMID:15145991

1. 3. ICP waveform disturbances

As ICP increases certain pathological waveforms can be observed on the ICP record. These abnormal waves are defined by their peak pressures and duration.
The waves described by Lundberg were:

- A waves or “Plateau waves” have amplitudes of 50–100 mmHg, lasting 5–20 min. These waves are always associated with intracranial pathology. During such waves, it is common to observe evidence of early herniation, including bradycardia and hypertension (Cushing response). The etiology is uncertain, but it is postulated that as CPP becomes inadequate to meet metabolic demand, cerebral vasodilatation ensues and CBV increases. This leads to a vicious hemodynamic circle with further CPP decrease.
- B waves have amplitudes up to 50 mmHg with a frequency 0.5–2/min and are thought to be due to vasomotor tone instability.
- C waves are up to 20 mmHg in amplitude and have a frequency of 4–8/min. These waves have been documented in healthy individuals and are thought to occur because of interaction between cardiac and respiratory cycles. Both A and B waves require intervention to reduce ICP and preserve CPP.

In text References

(LUNDBERG. 1960; Czosnyka and Pickard. 2004; Andrews and Citerio. 2004)

References

- Andrews PJ, Citerio G., Intracranial pressure. Part one: historical overview and basic concepts., 2004, PMID:15243684
- Czosnyka M, Pickard JD., Monitoring and interpretation of intracranial pressure., 2004, PMID:15145991
- LUNDBERG N., Continuous recording and control of ventricular fluid pressure in neurosurgical practice., 1960, PMID:13764297

1. 4. Indications for monitoring ICP patients with head injury

Note

Is raised ICP clinically important or an epiphenomenon?

While guidelines suggest that ICP monitoring should be instituted in all patients with severe head injury (Glasgow Coma Score <9) and positive findings on CT, all surveys or studies dealing with the real application of such guidelines show large variability in utilization, and an incidence of ICP monitoring markedly lower than expected.

Randomised clinical trials on the use of ICP monitors are difficult to design, as ICP monitoring is an accepted intervention for severely head-injured patients. Nevertheless, there is a conceptual agreement that ICP monitoring is not useful in patients who are considered to be unsalvageable. Other patients with less severe injuries, in whom a persistent increase of ICP is not expected, may not need a monitor.

A practical approach to decision-making in relation to whether or not an ICP monitor ought to be placed, is to develop local protocols defining:

- exclusion criteria
- situations where ICP monitoring is considered mandatory
- situations in which each case should be discussed individually.

Criteria of exclusion would be:

- patients with bilateral fixed pupils
- untreatable lesions at CT
- advanced age and comorbidities (controversial as there are studies showing reasonable outcomes in the elderly)
- extracranial lesion burden difficult to manage
- coagulopathy
- high GCS motor score (≥5).

ICP monitoring will be of higher yield where CT findings demonstrate a potentially evolving lesion or a diffuse pattern at risk for intracranial hypertension (i.e. obliteration of the third ventricle or compressed basal cisterns). ICP monitoring may be indicated in these situations even for patients with less severe neurological score (moderate head injury).

The appropriateness of ICP monitoring is uncertain (and will require individualised assessment and decision-making) where the lesion is less severe e.g. Diffuse Axonal Injury (DAI) grade 1, isolated traumatic subarachnoid hemorrhage (tSAH) without CT evolution at repeat CT, or isolated focal lesions in atrophic brains.

The flowchart below explains visually a potential method to approach the indication for ICP monitoring.

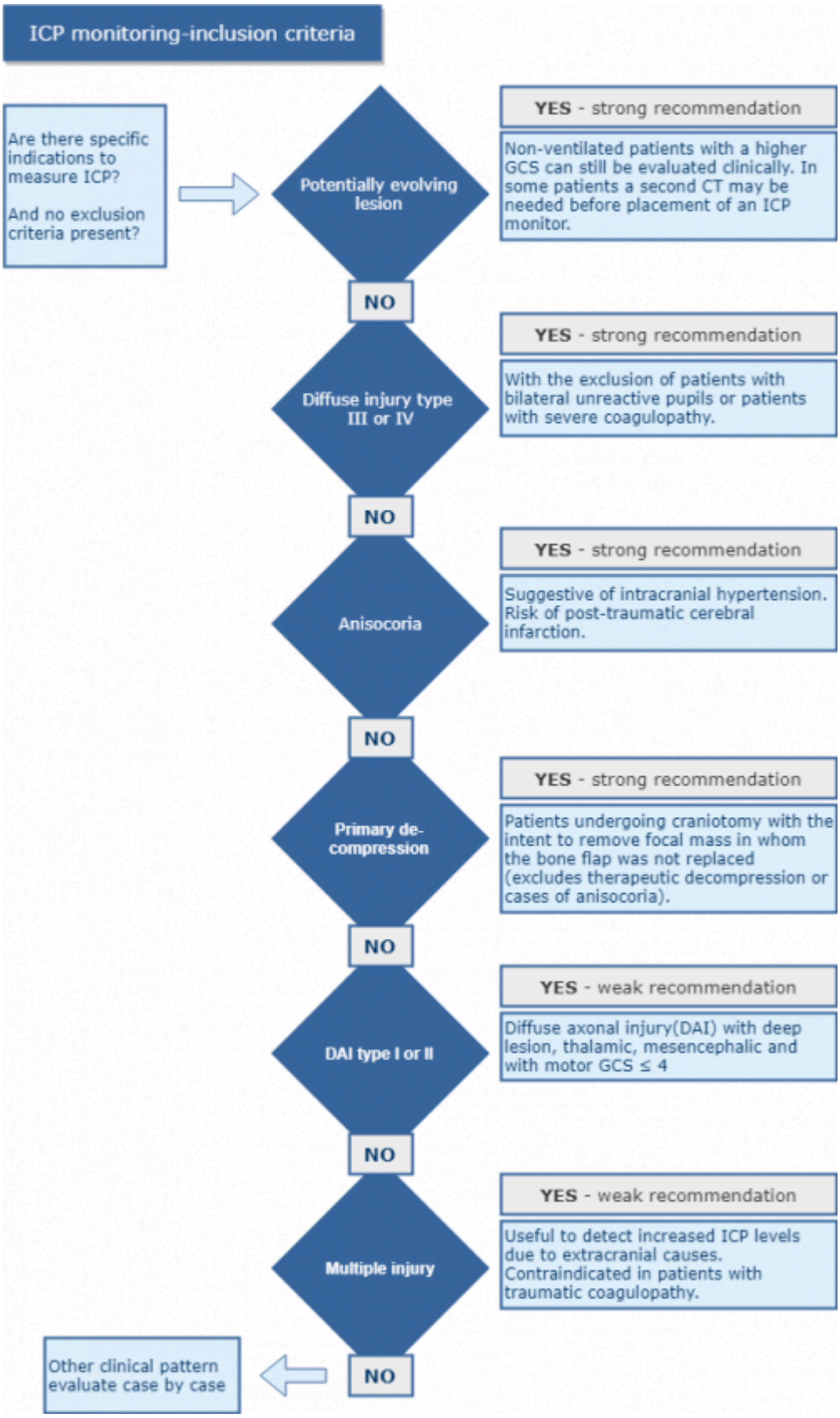

Figure 17: Proposed method to approach the indication for ICP monitoring: Indications.

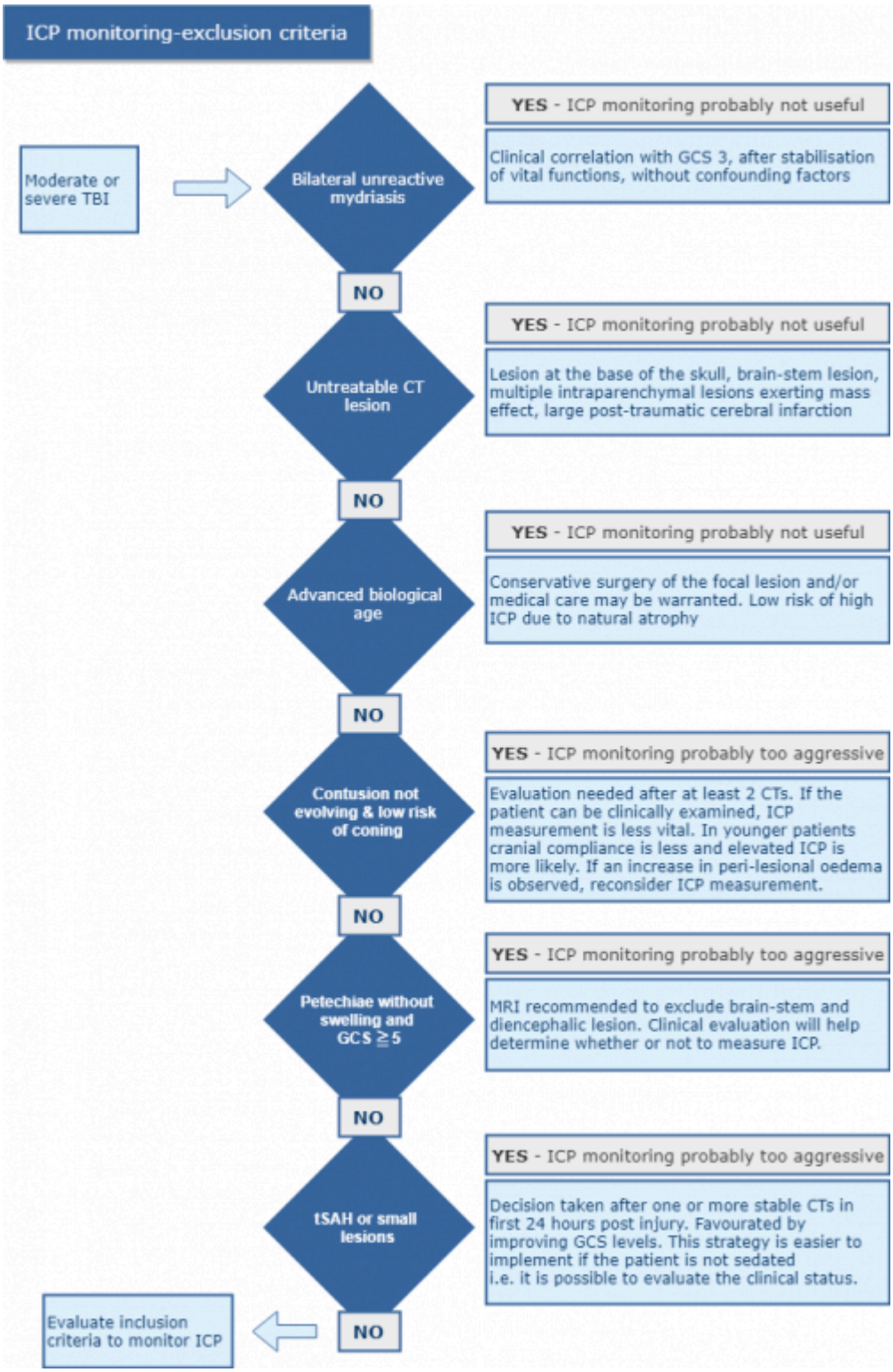

Figure 18: Proposed method to approach the indication for ICP monitoring: Contraindications

Challenge

Find out what proportion of head-injured patients with a GCS <9 in your institution have ICP measured. What is the indication for measuring ICP at your institution?

Task

Read studies of (Carney et al. 2017) reviewing the decline of mortality in association with introduction of measurement of ICP.

In text References

(Forsyth, Wolny and Rodrigues. 2010; Stein et al. 2010)

References

- Forsyth RJ, Wolny S, Rodrigues B., Routine intracranial pressure monitoring in acute coma., 2010, PMID:20166062
- Stein SC, Georgoff P, Meghan S, Mirza KL, El Falaky OM., Relationship of aggressive monitoring and treatment to improved outcomes in severe traumatic brain injury., 2010, PMID:19747054
- Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, Bratton SL, Chesnut R, Harris OA6, Kissoon N7, Rubiano AM8,9, Shutter L, Tasker RC, Vavilala MS, Wilberger J, Wright DW, Ghajar J., Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition., 2017, PMID:27654000

1. 5. Methods to measure ICP

As previously indicated, ICP can be measured by a variety of methods and in different anatomical sites. The methods include fluid-coupled systems with an external transducer, and fibre-optic and piezo-resistive systems. The parenchymal and intraventricular locations are the most commonly used anatomical sites (see figure 19).

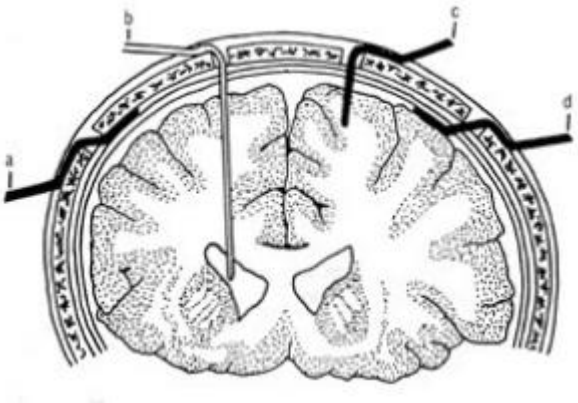

Figure 19: Invasive Methods to measure ICP: a: epidural, b: intraventricular, c: parenchymal, d: subarachnoid. Each has its advantages and disadvantages (see below).

Table 5: ICP measurement method: Advantages, complications and indications.

Method	Advantages	Problems	Indications/Contraindicatior

Ventricular	‘Gold standard’ Recalibration possible Reliable and cheap, CSF can be sampled and drained, can measure compliance	Infection, haemorrhage occlusion	Absolute contraindication: Uncorrected coagulopathy Relative contraindication: narrow or displaced ventricles
Parenchymal	Reliable Insertion simple	Recalibration not possible, expensive Infection (lower than ventricular), risk of haemorrhage (lower than ventricular)	Absolute contraindication: disturbances of blood coagulation
Epidural	Simple Low infection rate	Unreliable for long term monitoring	Relative contraindication: Uncorrecte coagulopathy

Challenge

You should observe the various techniques used to set-up ICP monitoring systems and observe how the measurement is used to influence individual patient care. What are the implications for your own practice?

In text References

(Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons; Joint Section on Neurotrauma and Critical et al. 2007)

References

- Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons; Joint Section on Neurotrauma and Critical Care, AANS/CNS, Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, Manley GT, Ne, Guidelines for the management of severe traumatic brain injury. VII. Intracranial pressure monitoring technology., 2007, PMID:17511545

1. 6. Threshold for ICP treatment

In the 4th edition of the Brain Trauma Foundation (BTF) guidelines, ICP monitoring is indicated in patients with severe TBI, because evidence suggests that ICP-guided treatment can reduce early mortality. The historical and most widely accepted ICP threshold for therapy is 20 mmHg, however the latest guidelines now recommend (level IIB) 22 mmHg. This approach, which is based on population targets, provides a generic universal threshold that potentially ignores patient-specific injury characteristics and host responses. Available published work suggests that there could be subtle differences in critical ICP thresholds between young and old, male and female patients, even at an aggregated population level, with older patients (age ≥55 years) and females having lower ICP thresholds (18 mm Hg vs 22 mm Hg) for prediction of poor outcome. Alternative approaches in individualizing the ICP threshold have been described based on advanced neuromonitoring. It has been suggested that the state of cerebrovascular pressure reactivity interacts with burden of intracranial hypertension in determining 6-month mortality; pressure passive conditions add vulnerability in the face of raised ICP, whereas states with preserved pressure reactivity may confer protection.

Task

Review this section in the BTF guidelines

In text References

(Sorrentino et al. 2012; Lazaridis et al. 2014)

References

- Sorrentino E, Diedler J, Kasprowicz M, Budohoski KP, Haubrich C, Smielewski P, Outtrim JG, Manktelow A, Hutchinson PJ, Pickard JD, Menon DK, Czosnyka M., Critical thresholds for cerebrovascular reactivity after traumatic brain injury., 2012, PMID:21964774
- Lazaridis C, DeSantis SM, Smielewski P, Menon DK, Hutchinson P, Pickard JD, Czosnyka M., Patient-specific thresholds of intracranial pressure in severe traumatic brain injury., 2014, PMID:24506248

1. 7. Threshold for CPP treatment

The recommended target cerebral perfusion pressure (CPP) value for survival and favorable outcomes is between 60 and 70 mm Hg. Whether 60 or 70 mm Hg is the minimum optimal CPP threshold is unclear and may depend upon the patient's autoregulatory status (level IIB, BTF 4th edition). One method for identifying, and

monitoring individualized optimal CPP (CPPOPT) at the bedside employs computerized derivation of a pressure reactivity index (PRx; a cross correlation coefficient among 30 consecutive, 10-second means of arterial blood pressure and ICP, ranging from -1 to +1); specialized software then allows for an automatic curve fitting of the relationship of different CPP ranges and PRx (by definition CPPOPT is the CPP range corresponding to the lowest part of this U-shape curve i.e. point of the curve with the lowest PRx observed). Retrospective analysis of prospectively collected data has shown that the difference between median CPP and CPPOPT, is an independent predictor of 6 month outcome.

Task

Review this section in BTF guidelines.

In text References

(Aries et al. 2012)

References

- Aries MJ, Czosnyka M, Budohoski KP, Steiner LA, Lavinio A, Kolias AG, Hutchinson PJ, Brady KM, Menon DK, Pickard JD, Smielewski P., Continuous determination of optimal cerebral perfusion pressure in traumatic brain injury., 2012, PMID:22622398

1. 8. Approach to the interpretation of ICP data

1. Check for neurological deterioration

Initially you have to evaluate if the ICP increase was associated with catastrophic brain herniation (new abnormal pupillary dilatation unreactive to light) or a consistent decline of GCS (if the patient is not sedated). If this is the case (though it is relatively infrequent) it is important to apply all efforts to reduce ICP immediately and plan a CT scan if an increase of mass effect (or a new mass lesion) is suspected.

2. Test if the increase of ICP is reliable

Excluding the above scenario, you should check the following points before any conclusion with a therapeutic implication is drawn.

- Can you recognise the pulsatile components of the ICP waveform?
- If you compress the external jugular veins (gently and briefly!), can you observe a rise in ICP?
- In the case of ventricular catheters: if you drain CSF, does the ICP decrease?
- Does the ICP value correspond with the clinical situation?

3. Evaluate the level reached by ICP elevation and its duration

ICP level can rapidly rise to very high levels. In such cases, CPP may decrease dramatically and the brain may become hypoperfused. However, most of these ICP waves are of short duration and due to hyperaemia waves in patients with abnormal, but not severely reduced, craniocerebral compliance. In such cases analyse rapidly the causes of easily avoidable ICP increases – see below.

4. Short lasting increase of ICP, hyperaemia waves

Causes of increased jugular venous pressure:

- Impaired drainage of blood at the neck: check the inclination of the head and that dressings do not compress the jugular veins (or have an inappropriately sized cervical collar).
- Increased intrathoracic pressure: avoid patient-ventilator dyssynchrony, exclude pneumothorax, haemothorax, pleural effusion. Decrease PEEP if oxygenation permits (usually PEEP<15 does not interfere with ICP, but this depends on lung and cranial compliances).
- Increased intra-abdominal pressure (IAP); measure IAP (bladder pressure) and apply corrective measures if possible when it is elevated.

Causes of increased arterial pressure and/or cerebral vasodilation:

- Check $EtCO_2$, as increased CO_2 may lead to cerebral vasodilatation. Check causes of pain and verify if the infusion pumps with analgesics are appropriately functioning. Use boluses of analgesics to test patient response.
- Verify any sudden increase or reduction of mean arterial pressure. An increase of MAP may be due to pain, ventilator-patient dyssynchrony, fever and shivering. A decline of MAP can be due to a malfunction of catecholamine syringe pumps or at pump change. Verify if the patient is shivering or if the temperature is rising. Treatment takes time and negative reactions to physical cooling must be avoided as well as any hypotension due to bolus doses of antipyretic. Low dose continuous infusion of diclofenac has been suggested for the management of fever.
- Verify if pupils are reactive and the patient's motor responses. Suspect crisis if posturing or seizures occur. Check EEG and deepen sedation.
- Check if a sudden reduction of SpO_2 occurred.

5. Rapid increase of ICP, high values, plateau waves, Lundberg A waves

Differing from, yet similar to, hyperaemia waves, small changes in intracranial volume, can provoke prolonged elevation of ICP once intracranial compliance is markedly reduced. This type of ICP elevation has been described by Lundberg as type A, and has a typical morphology characterized by a rapid rise of ICP until reaching a plateau which can last several minutes but usually ends rapidly with a return of ICP to previous values.

The physiology of plateau waves is complex and their impact on outcome uncertain.

In the plateau phase a reduced but preserved flow is still present due to vasodilation. This may explain why their impact as secondary insults is uncertain; however if untreated, brain herniation can occur during the plateau if the elevated ICP is long lasting. From a physiologic standpoint, onset of a plateau wave requires intact pressure reactivity that is later lost in a vicious vasodilatory cascade. A prompt reaction to rapidly rising ICP should aim introducing a cerebro-vasosconstrictive intervention, either directly (hyperventilation, indomethacin), or indirectly through metabolic coupling (barbiturate, propofol) or through autoregulation (vasopressors, mannitol, hypertonic saline).

6. Progressive increase of ICP due to systemic, potentially reversible causes

Frequently, ICP increases progressively over hours. Besides anatomical reasons, which are discussed below, a persistent state of hyperthermia, an absolute or relative hyponatraemia or status epilepticus may be associated with a prolonged increase in ICP.

7. Progressive increase of ICP due to intracranial causes – enlargement of perilesional oedema

In patients with traumatic contusions, after the first few days, it is common to observe an increase of perilesional vasogenic oedema (keep also in mind possible evolution of core haematoma). Management is guided initially towards preserving brain tissue by controlling ICP and increasing medical therapy - especially if the lesion is located in cortical areas associated with clinically important neurological functions (eloquent areas). If the ICP cannot be controlled by medical means, external decompression may be considered.

8. Progressive increase of ICP due to intracranial causes – worsening of diffuse swelling

An increase of cytotoxic oedema in patients with marked initial secondary insult, hypotension, cardiac arrest and worsened diffuse swelling may occur gradually over days. A further cause could be Post-Traumatic Cerebral Infarction, which may present after a time delay.

In text References

(Czosnyka et al. 1999; Castellani et al. 2009; Vespa et al. 2007; Bullock, Golek and Blake. 1989; Gutierrez et al. 2010)

References

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1. 9. The place of advanced monitoring techniques in head injury

Advanced neuromonitoring techniques which look at cerebral oxygenation, cerebral perfusion, and metabolism can give us deeper insight into the various pathophysiological mechanisms involved and help to individualize interventions.

1. 9. 1. Global measurement

ICP: Measurement of ICP remains the cornerstone of monitoring of patients with severe traumatic brain injury. When linked to MAP it provides a measurement of cerebral perfusion pressure. Global CBF seems to be dependent on CPP predominantly in the first hours post injury (there seems to be a matched drop in metabolic rate and correspondingly CBF). Conversely, in patients who survive and stabilise in ICU, CPP and global CBF are not correlated, probably as the result of preserved autoregulation and maintenance of CPP within autoregulatory range.

$SjvO_2$: While continuous $SjvO_2$ monitoring has not been shown to be of benefit, episodic $SjvO_2$ can detect, albeit infrequently, clinically occult episodes of global cerebral ischaemia and increased oxygen extraction, thus allowing, for example, the optimisation of hyperventilation in the treatment of intracranial hypertension. Infrequently, a decline of $SjvO_2$ is associated with very critical CPP and in such case is an ominous sign. Critical level of anaemia may be detected in association with low values of $SjvO_2$. Measurements of $SjvO_2$ have been largely replaced by measurement and monitoring or partial brain tissue oxygen tension ($PbtO_2$; should be appreciated that the latter is a focal indicator rather than a global one, such as $SjvO_2$).

In text References

(Macmillan and Andrews. 2000; Stocchetti et al. 2004)

1. 9. 2. Focal measurement

$PbtO_2$ and TD-rCBF: The apparent limitation of PbtO2 and rCBF (their regionality) is conversely the reason that they can be placed in perilesional oedematous regions. Here they can easily document how the penumbra is sensitive to changes of physiological variables. Recently, the Brain Tissue Oxygen Monitoring in
Traumatic Brain Injury (BOOST-2) trial was completed. It randomized 110 patients to treatment based on ICP monitoring alone (goal ICP <20mmHg) versus treatment based on ICP (goal <20 mm Hg) and PbtO2 (goal >20 mm Hg). The primary outcome was achieved with a median fraction of time with PbtO2 less than 20 mm Hg of 0.44 in the ICP group and 0.14 in the ICP/$PbtO_2$ group (P<.00001). There were no significant differences in adverse events and, protocol violations were infrequent. The BOOST-3 (phase 3) international, multicenter trial is now under planning.

In text References

(Longhi et al. 2007; Mulvey et al. 2004; Okonkwo et al. 2017)

Microdialysis: Is used clinically to estimate extracellular interstitial concentrations of small molecules (a standard 20-kDa nominal molecular weight cutoff membrane recovers glucose, pyruvate, lactate, glycerol, and glutamate), but can also be used to recover much larger molecules, such as inflammatory mediators from the interstitial fluid. The physiologic premise for obtaining tissue metabolic data rests on the assumption that it is critical to know when there is a transition from aerobic to anaerobic metabolism as a sine qua non of energy failure. This is signified by a biochemical pattern of increased lactate production and pyruvate consumption, leading to an increased LPR (thresholds of >25 or >40 have been used). Consequently, the LPR is thought of as a sensitive marker of brain redox state and secondary ischemic injury, and when raised has been associated with unfavorable clinical outcomes.

In text References

(Hutchinson et al. 2015)

1. 9. 3. Further monitoring

TCD: Transcranial Doppler may be better used in the non-invasive estimation of autoregulation. However it is operator dependent and relatively unstable. It is routinely applied in only a few centres. The pulsatility index can be used as an indirect surrogate for CPP adequacy (and/or intracranial compliance).

Continuous EEG monitoring may detect non-convulsive status epilepticus (NCSE).

Electrocorticography: is an invasive form of EEG monitoring where recording grids and strips are laid on the cortical surface intraoperatively. This technique affords more sensitive readings than surface EEG and allows the detection of self-propagating waves of neural and astrocyte depolarization, known as cortical spreading depression (CSD). These CSD waves lead to depressed spontaneous cortical activity for periods lasting minutes to hours. In experimental models of focal cerebral ischemia, the

presence of CSD has been associated with vasoconstriction, lesion expansion, and SBI. Spreading depolarizations have been also found to correlate with clinical outcome and be predictive of metabolic crisis, increased ICP, vasospasm, and delayed cerebral ischemia. Prolonged depolarizations are thought to reflect poor tissue perfusion and/or neurovascular uncoupling with disturbed flow autoregulation, and correlate with a worse prognosis in patients with TBI.

> **Think**
>
> In the absence of high quality prospective outcome data, is multimodality monitoring justified?

In text References

(Vespa et al. 1999; Hartings et al. 2011)

Neuroimaging developments: More recently neuroimaging modalities have been introduced in the diagnosis of specific pathophysiological conditions and their monitoring. These include:

- **CT perfusion:** A modified angio-CT in which a non-diffusible tracer is able to measure at high resolution regional CBF (rCBF) (quantitative) cerebral blood volume, and mean transit time. By comparing these different maps, an estimation of penumbral brain may be made. The absolute values of CBF should be evaluated with caution.
- **XeCT:** Xenon CT is a method to measure quantitatively regional CBF using Xenon as a contrast diffusible agent. Data results are highly reliable with a high spatial accuracy. It allows the combination of evaluation of rCBF with CT imaging. More recently the technique has been applied at bedside with the introduction of portable CT scanner.
- **PET:** A quantitative measurement of regional cerebral metabolic rate for glucose (rCMRG). In specialised centres with cyclotron, it can measure regional cerebral metabolic rate for oxygen (rCMRO2), regional CBV, regional oxygen extraction (rOEF), and regional distribution of benzodiazepine receptors (a marker of tissue viability). It is however a technique currently reserved for research centres. PET-CT can produce similar imaging coupled with a traditional CT.
- **MRI diffusion:** Quantifies with a ratio the typology of regional brain oedema, cytotoxic or vasogenic.
- **MRI perfusion:** Produces mapping of regional perfusion, and allows a description of penumbra, the area in which reduced perfusion is mismatched from the cytotoxic oedematous area.
- **MRI spectrometry:** Produce a semi-quantitative mapping of cerebral metabolites suggesting areas of ischaemia and excitotoxicity.

The place in clinical practice of standard and advanced monitoring techniques in TBI is further developed later.

In text References

(Wintermark et al. 2004; Chieregato, Tanfani and Fainardi. 2010; Coles. 2007)

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2. Treatment Of Severe Head Injury

The intensive care management of severe head injury consists of the provision of high quality general critical care and various strategies aimed at preventing or reducing secondary brain damage while the underlying pathology is resolving. Control of the factors involved in the ‘vicious cycle’ previously described is of specific relevance.

We shall deal firstly with the specific treatment strategies and conclude with comments on the general care of neurotrauma patients.

2. 1. Therapeutic intervention level

Most ICUs apply multi-tiered protocols to the care of increasing levels of intracranial hypertension. Correspondingly, a scale of therapeutic intervention has been developed. While these strategies are accepted worldwide, each centre has its own scale, in which barbiturate coma, mild to moderate hypothermia, mild hyperventilation, and decompressive craniectomy are considered controversial, higher tier therapies. It is helpful to audit the number and heterogeneity of ICP therapies regularly used within your ICU, both to monitor your own management and to improve communication among different specialists within the department and hospital.

In text References

(Stocchetti and Maas. 2014)

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2. 2. Specific management

This can helpfully be considered under four headings: surgery for haematoma; swelling of the brain; intracranial infections and seizures.

2. 2. 1. Surgery

Often immediate surgery is the primary treatment e.g. for large intracranial haematomas and contused brain lobes, and for depressed fractures and other penetrating injuries.

> **Think**
>
> In your daily practice, think about how decisions are reached about whether and when to operate; become involved in assessing and preparing patients before surgery and in their reassessment and post-operative care; and reflect on the issues surgery raises about effective communication among professionals and with families (see Patient Challenges and Early Management of Head Injury).

2. 2. 2. Swelling of the brain

According to the Brain Trauma Foundation guidelines, the critical values for specific intervention are: ICP >22 mmHg, and goal CPP 60-70 mmHg.

The conventional approach to the treatment of elevated ICP involves the sequential application of various treatment modalities, starting with basic and least invasive therapies.

2. 2. 2. 1. Basic treatment

Appropriate sedation and analgesia are critical since stress and pain may cause a rise in ICP. Mechanical ventilation is also mandatory, at least during the initial stages. The patient's head should be elevated at 30 degrees. Care should be taken to ensure that wound dressings and collars do not compress the jugular veins.

> **Think**
>
> Does analgesia and sedation in head-injured patients require a different approach from other trauma patients?

See ACE Course on Pain, Agitation and Delirium in Intensive Care for information.

2. 2. 2. 2. Standard interventions

2. 2. 2. 2. 1. Sedation

The endpoint of sedation should be to lower baseline ICP by decreasing the reaction of the brain to stimulation. In patients with reduced cranial compliance, the vasodilatation induced by stimulation may increase the cerebral blood volume and may lead to a persistent ICP elevation.

Conversely in patients with less severe injuries, and with enough preserved intracranial compliance, the level of sedation required may be lighter. Indeed in such cases the increases of ICP are self-resolving. Adequate levels of sedation may reduce the incidence of early seizures and non-convulsive status epilepticus. Finally sedation and analgesia can blunt autonomic responses to TBI.

In the few days after injury, in patients in whom there is chance of a prompt recovery, short-term sedative and analgesic regimens are suggested (propofol and remifentanil, or fentanyl). Conversely, in patients with severe CT findings, initial high ICP and at high

risk of secondary insults, neurological examination seems not to be of use and may be potentially dangerous. In such patients midazolam, and in more severe cases lorazepam, can be used as sedatives, with fentanyl as an analgesic. The half-life of each of them may be prolonged, especially in severely injured patients, when the duration of ICP instability is prolonged thus requiring these drugs to be infused for a number of days.

Once the ICP levels begin to be successfully controlled, daily sedation interruption may be useful to reduce the total dose. Alternatively, switching to as needed doses vs. continuous infusions has been shown to reduce the total amount given.

2. 2. 2. 2. 2. CSF drainage

For ICP ranging 20-25 mmHg, draining CSF via a ventricular catheter is a safe and generally reliable method of returning the value to more acceptable levels.

2. 2. 2. 2. 3. Mannitol

Administration of mannitol is an effective method to decrease ICP. Given intravenously it stays in the vascular compartment and creates a temporary osmotic gradient - osmolarity rises. Traditionally when serum osmolarity exceeds 320 mOsmol, administration of mannitol is stopped; nevertheless, little evidence exists in supporting the use of serum osmolarity for limiting mannitol dosing. A better strategy is to follow the osmolar gap (before the next dose) and trying to maintain it <20. Mannitol is given at doses of 0.5-1.5 gm/Kg anywhere from single as needed doses, to scheduled regiments of every 12 to every 6 hours. The are several risks from Mannitol administration including hypovolemia, acute kidney injury, and rebound cerebral edema.

Task

Test your knowledge

Sometimes treatment with mannitol is intensified in refractory cases (see the second patient in the 'Patient Challenges'). What is the main risk of this course of action to neurological and other pathology?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

A Rebound increase in ICP due to worsening of vasogenic oedema (because of the damaged blood brain barrier) and renal dysfunction.

2. 2. 2. 3. Second-line therapies

It is expected that patients who require these last tiers of therapies cumulatively are not more than 20–25% of the patients in whom ICP is measured. If higher rates pertain in a unit's audit of its practice, especially the rate of secondary decompressive craniotomy, then consideration is indicated to review whether this may represent failure of first level therapies and/or underuse of early surgery for mass lesions.

2. 2. 2. 3. 1. Hyperventilation

Hyperventilation acts fast, and efficiently in reducing intracranial hypertension; it should be one of the first maneuvers in acutely reversing transtentorial herniation ("buying time" in preparation for surgical evacuation of a mass lesion or for decompressive craniectomy). Hypocapnia causes cerebral vasoconstriction thereby lowering cerebral blood volume (and flow) and consequently ICP. If the reduction in CBF is not compensated by an increase of oxygen extraction, ischemic hypoxia may ensue. In general, hyperventilation has fallen out of favour (except for crisis situations as mentioned above); if used, $PaCO_2$ should not be allowed to fall below 30 mmHg. Also, it would be prudent to have monitoring of either SjO_2 or $PbtO_2$ when hyperventilating, in order to monitor for ischemic hypoxia.

Task

Test your knowledge

If you felt that a greater degree of hyperventilation was desirable, how might this be achieved with less risk of ischaemia?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Additional and more sophisticated monitoring of cerebral oxygenation might assist in this aim using techniques such as jugular bulb oximetry and brain tissue PO_2; see Neurological monitoring.

2. 2. 2. 3. 2. Barbiturates

High doses of barbiturates, such as pentobarbital and thiopental, reduce cerebral metabolism and lower ICP. As barbiturates have numerous side effects (e.g. hypotension, especially in volume-depleted patients, hypothermia, immunodepression and infection) they are only indicated as last tier (together with decompressive craniectomy- see RESCUEicp trial) when other treatments prove ineffective. Continuous EEG-recording is suggested to monitor their effects. The dose of barbiturate should be targeted to control ICP and not to reduce EEG activity.

Conversely, if ICP is unresponsive to barbiturates, further doses, once burst suppression has been already achieved, are inappropriate. The long half-life of barbiturates should be considered when infused even for a couple of days. Hypothermia, may lead to a further increase of barbiturate half-life due to depression of the hepatic metabolic rate.

Task

Test your knowledge

What particular type of infection is associated with the use of barbiturates in head-injured patients?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Respiratory infection.

Give two reasons why this might occur with barbiturates.

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Reduced respiratory ciliary activity and immune function.

2. 2. 2. 3. 3. Decompressive craniectomy

The present section discusses cranial decompression done to control refractory intracranial hypertension. This is called secondary decompression. Primary decompression is applied after primary surgery for mass effect.

Secondary decompressive craniectomy (DC) ‘to give the swollen brain more space’ is an effective method to lower ICP that has been shown to produce a worthwhile outcome in some cases. It serves as an advanced tier therapy’ and seems to be indicated especially when medical therapies fail to control ICP or the risk of associated complications become excessively high.

For patients with diffuse injury, the efficacy on long-term outcome of DC remains controversial. The reason may be that the TBI-associated axonal damage is in part independent from intracranial hypertension and/or that the complications associated with decompression may outweigh any immediate benefit on the intracranial pressure.

Secondary decompression, as with all second tier therapies, should be applied to most severe cases with persistently high ICP values, aiming for an acceptable disability or a good recovery. The extent of decompression should be large enough to avoid cortical ischaemia and venous engorgement in relation to the bone border.

There have been two multicentre randomized controlled trials that examined the role of DC for the management of refractory intracranial hypertension (DECRA-2011 and RESCUEicp-2016). These trials used different definitions of “refractory” ICP, had different sample size (DECRA also had a younger patient cohort), DECRA was only for diffuse TBI whereas RESCUE included focal injuries, and they were performed in different parts of the world. Overall, DECRA showed that DC for ICP control should not be done in an early aggressive fashion, since despite better ICP control did not lead to better outcomes. RESCUEicp showed significant mortality benefit for DC as compared to barbiturate coma (although that may be related to a higher than expected mortality for the control group). This survival benefit comes with a price of increased severe disability; for every 100 patients treated with DC rather than barbiturates, there were 22 more survivors; of these, 6 were in a vegetative state, and the other 16 were dependent on daily support for combinations of cognitive and physical disabilities. Surrogates of patients with refractory intracranial hypertension despite appropriate early tiers of therapy, should be informed of the ramifications of the above trials before deciding on the next best step.

In text References

(Stocchetti et al. 2005; Cooper et al. 2011; Hutchinson et al. 2016)

2. 2. 2. 3. 4. Hypothermia

Mild to moderate therapeutic hypothermia (HT) has been used to alleviate intracranial hypertension in traumatic brain injury (TBI). Its main contribution thought to be via reduction in cerebral metabolic requirement leading both to favorable oxygen/metabolic delivery-demand ratios as well as a reduction of cerebral blood volume resulting in decreased ICP. Nevertheless, HT is a clinically complex, labor-intensive procedure with numerous potential adverse effects. Furthermore, randomized controlled trials suggest either no effect or harm. These facts challenge the role of HT in TBI.

The most recent RCT evaluating HT for the control of ICP in patients with severe TBI is the POLAR study in 2018, in this trial 511 patients with TBI were randomized, from those, 266 were treated with prophylactic hypothermia (33-35°C for at leaste 72 hours) and 245 to normothermic management. They observed favourable ourcomes in 48,8% of the patients in hyportermia branch and 49,1% in the normothermic group with risk differences of 0,4% (95% CI, -9,4 to 8,7%) and rates of increased intracranial bleeding were 18,1% and 15,4% respectively concluding that prophylactic hypothermia in TBI patients did not improve neurologic outcomes in 6 months.

Before the POLAR study, the Eurotherm randomised more than 3000 patients with an ICP of more than 20 mmHg for ≥ 5 minutes despite stage-1 interventions (removal of space-occupying lesions, sedation, analgesia ± paralysis, maintenance of a mean

arterial pressure ≥ 80 mm Hg, and ventriculostomy), were randomized to either receive HT or to a control group that received stage-2 interventions without HT (osmotherapy and inotropes to maintain cerebral perfusion pressure ≥ 60 mm Hg). Mean daily ICP was similar in the two groups, however there were fewer occurrences of failure of stage-2 interventions to control ICP in the HT group, consequently more frequent use of stage-3 interventions (barbiturate-infusions, but not DC) was observed in the control group. The trial was stopped early owing to safety concerns; the results suggest that outcomes were worse with HT than with the treatment that the control group received. Based on the above, HT should not be used as an “early” intervention unless as a part of a clinical trial, although it may still have a role in patients with refractory intracranial hypertension.

In text References

(Andrews et al. 2015; Lazaridis and Robertson. 2016; Cooper et al. 2018)

2. 2. 3. Intracranial infections

Intracranial infections such as meningitis, brain abscess, and subdural empyema are complications of injuries which penetrate the dura mater and create a portal of entry for pathogenic bacteria such as depressed skull vault fractures, skull base fractures, and the injuries caused by stabbing, shooting or by a blast. It is most common when primary management of the wound has been deficient either because of limited healthcare resources or because the mechanism of injury has not been recognised.

Prevention of intracranial infections demands early recognition of risk followed by adequate surgical debridement of devitalised tissue, removal of foreign bodies, repair of the dura and skull, and the judicious use of antibiotics.

Most intracranial infections in TBI are avoidable. Septicaemia due to intracranial infections following TBI is extremely rare.

Task

Test your knowledge

Are prophylactic antibiotics of proven value in skull fracture? Explain your answer

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

A Not proven, by there is a recommendation (Grade 2C) for depressed skull fractures to receive prophylactic antibiotics for 5-7 days; regiment identical to the one recommended for penetrating head

trauma.

Outline possible collateral effects and considerations of prophylaxis in these circumstances – in relation to the patient and to the environment.

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Any approach with short-term prophylaxis should consider the impact on microbial ecology of the ICU and re-evaluate the cost-effectiveness of this approach. A further collateral effect of prohylaxis is to reduce the chance to detect early causes of patient infection in other site as the clinical picture will be obscured and because the induced bacteriostasis limits the growth of micro-organisms in laboratory culture.

The treatment of established intracranial infection may also involve the drainage of pus and the prolonged use of antibiotics as guided by cultures of pus, blood, CSF and clinical response.

Task

Test your knowledge

Which supplementary investigation would you use to monitor the efficacy of treatment and the need for further surgery?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Serial CT scanning would be the main method (with contrast to look for collections, alternatively Brain MRI with and without Gadolinium, and diffusion-weighted sequences).

Challenge

Ask your radiological colleague to show you some of the past series and relate these to the clinical findings.

2. 2. 4. Seizures

Seizures reflect disordered electrical discharges in the damaged brain. They are common after TBI (5–15% in various series), especially after operative haematoma evacuation, penetrating injury (including depressed skull fracture with dural penetration) and when there has been focal neurological signs or intracranial sepsis. Seizures can be classified as early or late (before or after seven days from the injury), and as generalised (grand mal) or focal. Repeated or prolonged seizures constitute status epilepticus. Late seizures imply a permanent risk of epilepsy and the need to consider long-term prophylaxis.

Prevention of seizures is the goal. Some drugs commonly used in the ICU should be avoided or used with caution. In 2018 Hazama A et al published a restrospective study based on 403 patients with TBI using Levetiracetam as early post-traumatic seizures phophylaxis observing non-statistically reduction in seizures incidence between the groups. Overal clinical studies found no diference in disability rating scale, mortality, seizures incidence or neurological outcome.

Challenge

Prepare a list of the drugs in common use in your ICU and determine which may provoke seizures. You may be surprised at how many such drugs there are.

Note

Usually in the clinical setting you cannot tell whether a certain drug is responsible for a seizure or whether it is ‘just the TBI by itself’. If a patient develops seizures following TBI – especially if they are pharmacoresistant – it is useful to remain aware of the possible predisposing influence of current medications and to consider discontinuing them where suspicion arises.

Anticonvulsants such as phenytoin and carbamazepine reduce the liability to early seizures (but not to late seizures), especially in high risk subgroups. Preventing intracranial infections is important.

In the conscious patient a single brief seizure may only require supportive treatment, but in the comatose patient every seizure can threaten life or function and should be treated. Seizures enormously increase the cerebral metabolic demand for oxygen, and raise ICP and lower CPP to critical levels by increasing CBF and by increasing CO_2 retention in spontaneously breathing patients.

Note

A seizure in the comatose patient is a life-threatening emergency.

Task

Test your knowledge

A head-injured patient, several hours after evacuation of a large extradural haematoma, has his sedation reduced to allow neurological assessment prior to extubation. He is observed to start having a generalised seizure. Presuming ABCs are addressed, outline your pharmacological approach.

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

An intravenous dose of lorazepam will probably abort the seizure. An intravenous infusion of phenytoin should then be commenced.

Outline your ongoing management of the phenytoin therapy?

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

Phenytoin should be loaded (20 mg/kg) at a max rate of 50 mg/minute. Then start a maintenance adult dose of 300 mg per day as guided by clinical response and the plasma level of the drug (may need to check free phenytoin levels, particularly in hypo-albuminemic patients).

If the patient's convulsions do not stop within 30 minutes, outline further pharmacological steps.

COMPLETE TASK THEN CLICK TO REVEAL THE ANSWER

This refers to an older definition of status epilepticus. Remember that the contemporary approach to status management defines it as either ≥5 minutes of continuous seizures or ≥2 discrete seizures between which there is incomplete recovery of consciousness.

In text References

(Carney et al. 2017; Hazama et al. 2018)

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