

BENEFITS AND DRAWBACKS OF CURRENT MONITORING MODALITIES IN TRAUMATIC BRAIN INJURY

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Monitoring plays a major role in the management of patients with traumatic brain injury (TBI) in an intensive care unit. Rational use of the monitoring depends on the benefits of these systems weighed against their pitfalls and risks. The following discussion deals with the benefits, risks and pitfalls associated with some of the major monitoring systems that are in current use in TBI.

General Systemic Monitoring

Unequivocal evidence exists at present about the role of secondary injury on the outcome of TBI. Systemic arterial hypotension and hypoxia are the two major determinants of poor outcome in these patients.¹ Optimization of cardiovascular and respiratory function is greatly aided by monitoring systemic parameters such as arterial blood pressure, central venous pressure, arterial oxygen saturation, blood gases, and urine output. Routine monitoring of biochemical parameters such as blood glucose, serum electrolytes, blood urea, serum creatinine and coagulation parameters is essential to optimize the systemic physiology and to promote the recovery of the injured brain. The complications associated with each of the above monitoring techniques and the pitfalls in analysis and interpretation of the results must be borne in mind while utilizing them in a head-injured patient.

Intracranial Pressure

Intracranial pressure (ICP) monitoring helps to optimize the cerebral perfusion pressure (CPP) in patients with TBI. Rigorous control of intracranial hypertension also prevents cerebral herniation.

Raised ICP is seen in 40% of patients admitted in an unconscious state and 50% of the mortality in severe head injury is associated with uncontrolled intracranial hypertension.² Intracranial hypertension accounted for 44% of the episodes of jugular venous oxygen desaturation in a prospective study of 116 patients with severe head injury.³

In the Traumatic Coma Databank (TCDB) series, the proportion of time the ICP was > 20 mmHg, and the proportion of time the mean arterial pressure (MAP) was < 80 mm Hg were two important predictive factors of outcome.⁴ In another large prospective cohort also ICP > 25 mm Hg, MAP < 80 mm Hg and CPP < 60 mm Hg were associated with poor outcome.⁵ In the data of the European Brain Injury Consortium (EBIC), intracranial hypertension was present in 55% of the patients in whom ICP was monitored, while it was suspected clinically only in 12% of the cases without ICP monitoring.⁶ All the above data suggests that continuous monitoring of ICP and a rigorous control of intracranial hypertension may favorably influence the neurological outcome after TBI.

Current Practices of ICP Monitoring in Head Injury

Over years, practices of ICP monitoring have varied greatly among various centres with some opting not to monitor ICP⁷ and others advocating its routine use in all cases.⁸

A 1991 survey of the centres that cared for head injured patients in the United States revealed that only 28% of the American neurosurgeons routinely used ICP monitoring. A large number of hospitals surveyed used ICP reducing measures such as hyperventilation and mannitol without monitoring the ICP.⁹ The acceptance and utilisation of ICP monitoring increased after the publication of the Brain Trauma Foundation (BTF) recommendations on management of head injuries in 1996.¹⁰ In a 1997 survey of 1239 neurosurgeons from the United States and Canada 83% felt that most patients with severe TBI should have ICP monitoring.¹¹ In fact, with recent literature emphasizing CPP-based management of severe head injury, ICP monitoring is becoming an integral part of the management of TBI. A Canadian survey published in 2000 revealed that, ICP monitoring was being used in more than 75% of the cases in 63% of the centres, in 50-75% of cases in 15% of the centres, in 25-50% of cases in 15% of the centres and in < 25% of cases in 7% of the centres.¹² Despite such high frequency of ICP monitoring, only 20% of the surgeons treating head injuries expressed a high level of confidence in ICP monitoring as a measure to improve the outcome; 23% expressed very low confidence and 56% expressed intermediate level of

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confidence. Seventy nine percent of the participants felt the necessity for a randomized controlled study.

In the United Kingdom, ICP monitoring rates are only about 50% in the neurosurgical centres.^{13,14} In a survey of 67 centres in 12 European countries also, ICP monitoring was used only in 37% of the cases.⁶ A 2003 report from France has shown that 44% of the trauma centres could not monitor ICP for want of a neurosurgical facility in their hospital while all the hospitals with available neurosurgical facility did monitor ICP¹⁵ Thus, there seems to be a great variability in the incidence of ICP monitoring among various centres treating TBI.

Effect of ICP Monitoring on Outcome

The impact of ICP monitoring on outcome of head injury has never been investigated systematically due to methodological difficulties. It has been estimated that a sample size of 768 patients is required to prove a reduction in mortality from 35% to 25% with an alpha of 5% ($p < 0.05$) and a beta of 20% (power of 80%).¹⁶ Studies of this magnitude consume time and require major financial resources. Since ICP monitoring has become an integral part of head-injury management in many major centres, and most experts consider it indispensable, it is also difficult to design a randomized study.

Evidence in Favor of ICP Monitoring

In 1977, Jennett et al reported a mortality of 50% in patients with a GCS of ≤ 8 for at least 6 h.¹⁷ This was soon followed by reports of a significant reduction in the mortality to 30% with an intensive management protocol that included ICP monitoring.^{18,19} Saul and Ducker, in a prospective study of patients with a GCS ≤ 7 treated the initial 127 patients with an ICP threshold of 20-25 mmHg; in the next 106 patients, the ICP threshold was brought down to 15 mmHg. The mortality was 46% in the former group and 28% in the latter ($P < 0.0005$).⁸ Eisenberg et al used pentobarbital to treat intractable intracranial hypertension unresponsive to conventional measures. Survival rates were 92% when the ICP could be controlled and 17% when the ICP could not be controlled.²⁰

In a 1989 study comparing the management of head injuries in Charlottesville, Virginia, USA and New Delhi, India, there was no overall difference in outcome between the two institutions.²¹ However, in a subgroup of patients with a Glasgow Motor Score of 5, mortality in Charlottesville was 4.8% as against 12.5% in New Delhi. This difference was attributed to better critical care including ICP monitoring in Charlottesville.

A 36% mortality rate was reported from TCDB cohort comprising of four research centres in the United States where ICP monitoring is a routine.⁴ This mortality was significantly lower than what has been reported in earlier studies without ICP monitoring.

In an analysis of the data files of the Ontario Trauma Registry from 1989 to 1995, ICP monitoring was associated with a significantly improved survival.²² In a non-randomized study of head injuries with a GCS ≤ 7 by Ghajar et al, thirty-four patients were treated with ICP monitoring and 15 without ICP monitoring; mortality was 12% in the monitored group and 53% in non-monitored group.²³ The results of all the above studies suggest a beneficial role for ICP monitoring.

Evidence against Benefits of ICP Monitoring

In a randomized controlled trial of 80 patients with severe head injury by Smith et al,²⁴ one group received mannitol 0.25 g/kg for ICP > 25 mm Hg and pentobarbital for ICP > 35 mmHg; the other group received mannitol 0.25 g/kg/2 h empirically. Mortality rates were 35% and 42% with and without ICP monitoring respectively suggesting the futility of ICP monitoring. The difference was not statistically significant. In 1983, an Australian study of 100 severe head injuries without ICP monitoring reported a mortality of 34% and favorable outcomes in 49% of the patients, rising doubts about the value of ICP monitoring.⁷ In a more recent study of 37 patients with severe head injury and uncontrolled intracranial hypertension for more than 96 h, age of the patient and the GCS at admission were the only predictors of good outcome. No difference was found between patients with good and poor outcomes in terms of the mean or peak ICP, percentage of time with elevated ICP, lowest CPP or the length of ICP monitoring, questioning the role of ICP monitoring.²⁵

Recommendations of the Brain Trauma Foundation

The Brain Trauma Foundation (BTF) and the American Association of Neurological Surgeons (AANS) summarised the available evidence and formulated recommendations for ICP monitoring in TBI. Based on the class of evidence, the recommendations were divided into standards, guidelines and options. The review concluded that there is no class I evidence based on which standards could be laid down. The recommendations of BTF and AANS are as follows.²⁶

A. Standards :

There are insufficient data to support a treatment standard.

B. Guidelines:

- i) ICP monitoring is appropriate in patients with severe head injury with an abnormal admission computed tomographic (CT) scan. Severe head injuries are defined by a GCS of 3-8 after cardiopulmonary resuscitation. An abnormal CT scan of the head is one that reveals hematomas, contusions, edema or compressed basal cisterns.
- ii) ICP monitoring is appropriate in patients with severe head injury with a normal CT scan if two or more of the following features are noted at admission: age over 40 years, unilateral or bilateral motor posturing, systolic blood pressure < 90 mmHg.
- iii) ICP monitoring is not routinely indicated in patients with mild or moderate head injury. However, a physician may choose to monitor ICP in certain conscious patients with traumatic mass lesions.

The cochrane database review

A recent Cochrane database review addressing the need for routine ICP monitoring found no trials to show the effects of routine monitoring of ICP following head injury.²⁷ The review suggests the need for more research. But randomised trials of management with or without ICP monitoring are unlikely to be carried out for ethical reasons. For similar reasons trials of ICP monitoring with and without treatment are also unlikely to be undertaken.

The pitfalls of ICP monitoring are related to the complications associated with the technique employed. In one study, ventriculostomy had a higher rate of complications and higher incidence of infections than intra parenchymatous ICP devices (12.4% vs 1.2%);²⁸ the Glasgow Outcome Score was worse if complications were present. In 68 probe tips of the Camino fiberoptic device, Martinez-Mañas et al.²⁹ found that contamination is frequent (13.2%) but without clinical relevance; only 2.9% of the cases needed treatment. All were related to time of monitoring (more than 10 days). When clinically relevant hemorrhage appeared, it was related to previous coagulopathy.

Jugular venous oximetry

Reflectance oximetry, by using a fiberoptic catheter has allowed continuous monitoring of jugular venous oxygen saturation (SjvO₂). In patients with bilateral brain injury, the catheter is usually placed in the internal jugular vein on the side of dominant drainage, usually the right.^{30,31} In the presence of a focal brain injury, it is controversial if the catheter should be placed on the side ipsilateral to brain injury or on the dominant side, if different. The dominant side may be determined by comparing the ICP

increase caused by manual compression of each internal jugular vein,³² by computed tomographic assessment of jugular foramen size,³³ or by ultrasonography to compare internal jugular vein size.

SjvO₂ is an indirect measure of cerebral oxygen use. When demand exceeds supply, the brain extracts greater oxygen, resulting in decreased jugular bulb oxygen saturation. If cerebral blood flow (CBF) decreases, a point is eventually reached at which the brain can no longer completely compensate for decreased CBF by a further increase in oxygen extraction. At this point, oxygen consumption decreases and anaerobic metabolism with lactate production ensues. When cerebral oxygen supply exceeds demand, oxygen saturation of jugular bulb blood is increased.

The arteriovenous oxygen difference in brain [(A-V) DO₂] is normally stable at 4-8 mL O₂/100 mL blood. If cerebral oxygen consumption (CMRO₂) remains constant, changes in (A-V) DO₂ should reflect changes in CBF. If (A-V) DO₂ is < 4 mL O₂/100 mL blood, it is assumed that oxygen supply is greater than demand (i.e., luxuriant). An (A-V) DO₂ > 8 mL O₂/100 mL blood suggests that demand is in excess of supply (i.e., ischemia). If CMRO₂ increases without an increase in CBF, the brain extracts more oxygen from the blood, and there is a decrease in oxygen content or saturation of the venous blood from the brain. The normal value for SjvO₂ is approximately 55%-75%.

In the setting of TBI, SjvO₂ monitoring provides an early diagnosis of ischemia resulting from either intracranial or systemic causes.^{34,35} Moreover, SjvO₂ monitoring may be useful to guide decisions for optimizing hyperventilation therapy,³⁶ guiding fluid management and oxygenation,³⁷ and optimizing perfusion pressure.^{38,39} Used with a transcranial Doppler (TCD) monitor, SjvO₂ can help to distinguish cerebral hyperemia from vasospasm. With high flow velocity detected by transcranial Doppler, SjvO₂ is increased during hyperemia and normal or low if cerebral vasospasm is present.

Barbiturate coma and therapeutic hyperventilation are examples of therapies for head injury that may be guided by SjvO₂ monitoring. Cruz⁴⁰ identified a group of head-injured patients who responded to pentobarbital with a decrease in SjvO₂. It was hypothesized that the vasoconstrictive effect of barbiturates resulted in increased cerebrovascular resistance and oligemic cerebral hypoxia in these patients.

The contemporary guidelines of head injury management recommend "optimal hyperventilation" guided by SjvO₂ monitoring, thus identifying those head-injured patients with the potential for an ischemic response to hypocapnia.

Relative contraindications to $SjvO_2$ monitoring include a cervical spine injury, and presence of a tracheostomy or a coagulopathy. Complications of $SjvO_2$ monitoring are uncommon and related to catheter insertion. Complications include carotid artery puncture, pneumothorax, nerve injury, infection, and thrombosis. The concern that a jugular catheter might obstruct venous return and increase ICP appears to be unfounded.

Another limiting factor in the acceptance of $SjvO_2$ monitoring has been the relatively poor correlation of concomitant values obtained from cerebral oximetry catheters to an internal jugular venous sample analyzed by a co-oximeter for oxygen saturation. When used in the venous system with non pulsatile, retrograde flow and a vessel wall that is susceptible to catheter abutment, there have been limitations in the correlation of the online saturation value to oxygen saturation measured by a co-oximeter. These concerns, although still present, have been addressed by recent technologic advances.⁴¹

Concerns have been expressed on the possibility of contamination of the jugular bulb blood flow with extra cerebral blood flow during sampling. If blood is sampled at a site within 2 cm of the jugular bulb and at a rate of < 2 mL/min there is negligible (approximately 3%) extra cerebral contamination.⁴² A related concern is the observation that, as CBF decreases the relative extra cerebral contribution to $SjvO_2$ reading increases. A final technologic issue is the concern of catheter migration and abutment against the vessel wall. Distinguishing a "desaturation reading" as a result of a change in position of the catheter tip from a pathologic desaturation can be problematic. Because of the above concerns, cerebral oximetry catheters have to be routinely calibrated to a co-oximeter control.

$SjvO_2$ is a measure of global cerebral oxygenation and is not particularly sensitive to small areas of focal ischemia.⁴³

Transcranial doppler

Transcranial Doppler (TCD) ultrasonography is a non-invasive monitor providing indirect information of cerebral blood flow in one of the major arteries in the base of the brain. A 2 MHz pulsed ultrasound signal is transmitted through the skull (usually through the temporal bone) and the red cell flow velocity (FV) is measured by using the Doppler shift principle. Insonation of one of the arteries (most commonly the middle cerebral artery (MCA)) produces an arterial waveform giving information on systolic, diastolic and mean blood flow velocity. The mean flow velocity (FV mean) is a weighted mean velocity that takes

into account the different velocities of the formed elements in the blood vessel insonated and normally has a mean value of 55 ± 12 cm/s in the MCA. Changes in FV correlate closely with changes in CBF provided the angle of insonation (the angle between the axis of the vessel and the ultrasound beam) and the diameter of the vessel insonated remain constant. In the absence of vessel stenosis or vasospasm or changes in arterial blood pressure or blood rheology, the pulsatility reflects the distal cerebrovascular resistance. This resistance is usually quantified by the Pulsatility Index (PI or Gosling index) = $(FV_{sys} - FV_{dias}) / FV_{mean}$. The PI (normal PI ranges from 0.6 to 1.1) has been shown to correlate with CPP.

One of the most useful applications of TCD in head injury is in the diagnosis of high velocity states such as cerebral vasospasm or hyperemia. The differentiation between the two conditions is important in order to target therapy more appropriately. Flow velocities of greater than 120 cm/s after insonating the MCA is considered significantly high. If the ratio of MCA flow velocity to extracranial internal carotid flow velocity (Lindgaard ratio) is greater than 3, vasospasm is the likely diagnosis, whereas if mean MCA FV > 120 cm/s and the Lindgaard ratio is less than 3, hyperemia is diagnosed.

Following traumatic brain injury, TCD monitoring can be used to observe changes in FV, waveform pulsatility and for testing cerebral vascular reserve. TCD has also been used to measure ICP and CPP non-invasively.^{44,45} This is useful in patients where placement of invasive devices is a contraindication. Ex: coagulopathy. In addition, by continuous recording of the FV_{mca}, the auto regulatory 'threshold' or 'break point' (the CPP at which autoregulation fails) can be easily detected, providing a target CPP value for treatment. Autoregulation can be tested by response of the TCD trace to vasopressor infusion (static autoregulation) or thigh tourniquet deflation (dynamic).

The major limitation of the TCD lies in the fact that what it measures velocity and not flow. Secondly, the values are heavily operator-dependent. Continuous monitoring is not possible, though recently head frames are available with which the probe can be placed in position and data acquired over a long period.

Brain tissue oxygenation

Cerebral ischemia is common in head-injured patients. It appears early following trauma. To detect and treat the brain tissue hypoxia as soon as possible, different groups have used micro sensors placed into the brain parenchyma and monitored the brain tissue partial oxygen pressure (Pbt_iO₂) continuously. In 101 comatose

patients, the use of Pbt_iO₂ was beneficial in the clinical management of the patients. Pbt_iO₂ had a good relation with the outcome. If Pbt_iO₂ was less than 10 mmHg for more than 30 minutes, the odds ratio for unfavorable outcome was 2.8 (95% CI, 1.2–6.3). This odds ratio is similar to that of other powerful predictors such as age, GCS score, and pupil reactivity.^{46,47}

Pbt_iO₂ and SjvO₂ were compared in some studies. Kiening et al⁴⁸ showed, in 15 patients in whom both parameters were placed simultaneously, that, first of all, good quality data were obtained 95% of the time with Pbt_iO₂ and only 43% of the time with SjvO₂. Second, they found a good correlation between different CPP values and both neuromonitoring parameters (Pbt_iO₂ and SjvO₂), and suggested that all their patients had preserved autoregulation and that a CPP of 60 mmHg would be enough. Gopinath et al⁴⁹ monitored SjvO₂ and Pbt_iO₂ in 58 head-injured patients and concluded that SjvO₂ presented good quality data 90% of the time, as Pbt_iO₂ did. The reduction in CBF, decreasing PaCO₂ from 36 to 26 mmHg, was better detected by SjvO₂. Pbt_iO₂ also decreased, but not in all patients, and in some even increased. These findings were probably related to disturbed vascular reactivity, when lowering PaCO₂, in areas with focal pathology. With different patterns, both parameters detected the global cerebral ischemia.⁴⁸

When the inspired oxygen concentration was changed from 40 to 100%, the Pbt_iO₂ better reflected the modification, as other studies show.⁵⁰ This could have therapeutic relevance to improving cerebral oxygenation in areas that are suffering tissue hypoxia, and then shifting the metabolism from anaerobic to aerobic.

Also, Pbt_iO₂ seems to work properly as a prognostic index, as it detects brain hypoxia. In 43 patients, Valadka et al. demonstrated that low Pbt_iO₂ (less than 15 mmHg) and the length of time (greater than 30 min) it remained low are correlated with outcome.⁵¹

There is some controversy about the site for placement of the probe. Probably where the probe must be placed is in the “penumbra zone” or even in undamaged brain tissue, because the therapy can be better directed.

Continuous Pbt_iO₂ measurements also are useful in the management of CPP and other therapies, because they allow one to detect the benefit, or not, of every change in treatment.⁵² Where to place the limit under which the brain tissue can be considered to be suffering hypoxia is still unclear. Many authors find different cut-points.⁵³ Probably when the Pbt_iO₂ level is below 15 mmHg, the brain tissue is at risk of being damaged.

The Pbt_iO₂ measurement gives good quality information about brain tissue oxygenation, and its measure is complementary to that given with jugular bulb oxygen determinations and gives the chance for better patient management.

Laser doppler flowmetry

Laser Doppler flowmetry (LDF) is a technique that tries to continuously assess the current status of the microcirculatory flow. Data obtained by this method seems to have a good correlation with the CBF measured by other methods.⁵⁴ In twenty-six head-injured patients tested for autoregulation with this tool⁵⁵ good correlation was found between the data obtained by this technique and traditional measures, with only 3% discordance. Studies based on LDF⁵⁶ recommend a careful manipulation of CPP in the presence of disrupted autoregulation.

The problem with this technique is that the probe shifts easily, the technique can only assess the CBF in a small volume of tissue, the measure is not quantitative, and artifacts could be produced by a large numbers of external derangements.

Near infrared spectroscopy

The principle of Near Infrared Spectroscopy (NIRS) is based upon the fact that light in the near infrared red range (700-1000 nm) can pass through the skin, bone and other tissues relatively easily. When a beam of light is passed through brain tissue, it is both scattered and absorbed. The absorption of near infrared light is proportional to the concentration of certain chromophores, notably iron in haemoglobin and copper in cytochrome aa3. Oxygenated haemoglobin (HbO₂), deoxygenated haemoglobin (Hb) and cytochrome aa3 have different absorption spectra, depending on the substances' oxygenation status. Changes of concentration of near infrared light as it passes through these compounds can be quantified using a modified Beer-Lambert law, which describes optical attenuation. The main advantage of NIRS is that it is a non-invasive method of estimating regional changes in cerebral oxygenation. With recent technological advances, it is possible to measure regional CBF⁵⁷ and regional CBV⁵⁸ although the technique is not well validated.

The clinical use of NIRS is limited by its inability to differentiate between intracranial and extracranial changes in blood flow and oxygenation which adversely affects the reliability of the readings.⁵⁹ The validation of this technique in neurointensive care still requires further work.

Electrophysiology

An electroencephalogram (EEG) represents spontaneous electrical activity of the cerebral cortex. It does not reflect activity in subcortical levels, cranial nerves or the spinal cord. The electrical activity is recorded from scalp electrodes. The electrical signal is amplified, filtered and then displayed as either 8 or 16 channels (8 channels per hemisphere) to give an accurate representation of electrical activity throughout the cortex. EEG activity is usually interpreted in terms of frequency, amplitude, and location (focal or generalized activity). To facilitate continuous EEG monitoring several automated EEG processing systems have been developed. Power spectral analysis allows fast Fourier transformation of small intervals of EEG to provide a graphical representation of the relative power content of the various frequency bands in each segment of EEG. These spectral diagrams are then stacked to show how the frequency of the EEG alters with time to produce a compressed spectral array. This spectral analysis can also give a single number (either the mean frequency or the frequency below which 95% of the signal lies) that can be tracked over time.

EEG is an important tool in the investigation and management of seizures associated with head injury, especially in patients who are paralysed and mechanically ventilated. EEG plays an important role in the detection of non-convulsive seizures. Seizures can occur in 20% of the patients with TBI admitted to intensive care units.⁶⁰ Majority of these seizures is of non-convulsive in nature and occurs in spite of adequate serum concentration of anticonvulsants. In these situations EEG plays a pivotal role in identifying seizures and thereby preventing secondary damage to brain. Continuous EEG monitoring is also useful in detecting ischaemic cerebral events, arising from intracranial hypertension after head injury.⁶¹ Certain EEG features are associated with a poor outcome and in some cases may be useful in predicting eventual survival. Various grading systems have been developed based on the presence or absence of these features. Metabolic suppression using intravenous anaesthetic agents may be monitored using EEG, where burst suppression or isoelectricity is a useful endpoint to obtain maximal suppression of cortical electrical activity.

The limitations of EEG monitoring in head injury are as follows: It may be difficult to obtain a noise-free signal in the intensive care unit. The information obtained from EEG does not help to assess the function of the subcortical structures. Interpretation of the voluminous information generated requires an experienced electrophysiologist.

Microdialysis

The fundamental principle of microdialysis is to measure the concentration of chemicals in the extracellular space of the brain by mimicking the action of a blood capillary. In practice, a fine tube (diameter 0.62 mm) lined with polyamide dialysis membrane is placed directly into the brain and is perfused with a physiologic solution (e.g., Ringer) at ultra low flow rates (0.1–2.0 $\mu\text{L}/\text{min}$) using a precision pump. Molecules below the cutoff size of the semipermeable membrane (approximately 20,000 daltons) diffuse from the extracellular space into the perfusion fluid, which is then collected into vials that are changed every 10 to 60 minutes. The samples are analysed in the laboratory. The major difficulty with microdialysis is that an analysis of very small volumes (<10 μL) is required. Newer microdialysis analyzers (CMA Microdialysis, Stockholm, Sweden) have on-line measurement of glucose, lactate, pyruvate, glutamate, and glycerol in the intensive care unit or operating theatre. Good correlation has been shown between the CMA600 analyzer and the gold standard of high performance liquid chromatography.⁶² Various case reports have shown correlations between adverse clinical events, such as high ICP, low blood pressure, hypoxia, high lactate, low glucose, high antioxidant levels and high excitatory amino acid (EAA) levels. Correlations have been demonstrated between jugular bulb oxygen desaturation, lactate and glutamate;⁶³ and between jugular bulb desaturation, lactate, adenosine, and xanthenes.⁶⁴

Various studies have looked at the effects of interventions on levels of extracellular chemicals after head injury. Thiopental coma was associated with a reduction in lactate, glutamate, and aspartate.⁶⁵ Hypothermia significantly reduced glutamate and aspartate levels in six patients.⁶⁶ Hyperoxia led to a reduction in lactate in 14 patients.⁶⁷ The Lund group showed a reduction in lactate, glutamate, lactate/pyruvate ratio, and glycerol after a controlled reduction in the cerebral perfusion pressure according to the Lund protocol.⁶⁸

One of the problems with microdialysis is that the concentration of substance in the microdialysate does not necessarily equate to the true extracellular concentration. There are many pitfalls and limitations of microdialysis. The catheter insertion causes some disruption of local tissues. The probe may induce spreading cortical depression, reduced cerebral blood flow, reduced glucose phosphorylation, and uncoupling of flow and metabolism for the first 24 hours. Probe insertion may cause small hemorrhages into the catheter tract, mild astrogliosis, and macrophage infiltration. After several days, reticular fiber deposition and gliosis have been shown to occur in

animals, which may affect the performance of the catheter.⁶⁹ As the normal values of microdialysis are tentative, cut off values that can predict poor outcome are still not well defined.

Bispectral index (BIS)

There are a few studies of the role of bispectral index in head injury. BIS scores obtained prior to sedation in patients of trauma, have been found to be predictive of TBI and neurological outcome at discharge in one study.⁷⁰ In this study, BIS values were monitored at the time of admission. Pre-sedation BIS values were correlated with computed tomographic evidence of TBI. The probability of recovery from unconsciousness based on BIS monitoring was investigated by Fabregas et al in 25 patients with brain injury; statistically significant differences of BISmax, BISmin and BISmean were found between patients who recovered consciousness and those who did not.⁷¹ BIS scores and GCS were assessed for 20 min for each patient and these scores were correlated with the Glasgow Outcome Scale (GOS) at six months. The study population in this report, of course, consisted of patients with various other types of pathology also in addition to TBI. Among the patients with TBI there were both diffuse and focal injuries. In our own study limited only to patients with mild and moderate TBI, we correlated BIS and GCS values measured over a period of 10 days in the scenario of changing clinical status of the patient. The results showed a correlation of BIS with GCS. However, the scatter of BIS values for any GCS score was high limiting the value of BIS in predicting GCS. Mean BIS values were significantly different between mild and moderate head injuries [65.7 ± 16.1 vs 85.7 ± 6.1 , $p = 0.006$].⁷²

Multimodality monitoring

The concept of multimodal monitoring involves continuous monitoring of more than one parameter using two or more of the techniques described above. This helps to overcome the limitations of each individual method of monitoring thereby enabling more accurate analysis of changes in the measured parameters. For example, a change in the ICP associated with an increase in CBF or ischemia can be accurately interpreted when TCD flow velocity information is combined with ICP data. The use of multimodal monitoring has some disadvantages. As multiple monitors are used, the system becomes more expensive. The complex systems involved also require highly trained staff to maintain the various modalities and ensure that the monitors are correctly placed at all times. The data generated needs to be acquired in a format that allows

quick and easy analysis. Computer support for downloading the data is an essential part of the system.

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