INTERNATIONAL JOURNAL OF
CLINICAL NEUROSCIENCES
AND MENTAL HEALTH

REVIEW

Multimodal brain monitoring in neurocritical care practice

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Special Issue on Neurosonology and Cerebral Hemodynamics

Abstract

The management of severe acute neurological patients is a constant medical challenge due to its complexity and dynamic evolution. Multimodal brain monitoring is an important tool for clinical decision at bedside. The datasets collected by the several brain monitors help to understand the physiological events of acute lesion and to define patient-specific therapeutic targets. We changed from pure neurological clinical evaluation to an era of structure and image definition associated with instrumental monitoring of pressure, flow, oxygenation, and metabolism. At each time, we want to assure perfect coupling between energy deliver and consumption, in order to ensure adequate cerebral blood flow and metabolism, avoid secondary lesion, and preserve normal tissue.

Continuous monitoring of intracranial pressure, cerebral perfusion pressure, and cerebrovascular reactivity with transcranial Doppler, allows us to predict cerebral blood flow. However, adequate blood flow means not only quantity but also quality. To study and avoid tissue hypoxia we start to use methods for evaluation of oxygen extraction, such as oxygen jugular saturation, cerebral transcutaneous oximetry or measurement of oxygen pressure with intraparenchymal probes. To better understand metabolic cascade we use cerebral microdialysis to monitor tissue metabolites such as glucose, lactate/pyruvate, glycerol or cytokines involved in the acute lesion. Multimodal brain monitoring in neurocritical care practice helps neurointensivists to better understand the pathophysiology of acute brain lesion and accomplish the challenge of healing the brain and rescue lives.

Keywords: Multimodal brain monitoring, Intracranial pressure, Cerebral oximetry, Cerebral oxygenation, Cerebral blood flow, Cerebral microdialysis, Cerebrovascular reactivity indexes, Neurocritical care.

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Citation: Dias, C. Multimodal brain monitoring in neurocritical care practice. IJCNMH 2014; 1(Suppl. 1):S08

Received: 01 Sep 2013; Accepted: 29 Oct 2013; Published: 09 May 2014

Introduction

The main purpose of neurocritical care is to fight brain cell death, giving adequate flow, oxygen, and glucose in order to promote neuronal, endothelial, and glial cell recovery to ensure neuronal function. Although clinical evaluation of comatose patients is still one of the foundations of clinical neuroscience, the neurological findings of adverse events appear too late in time. Multimodal brain monitoring may give crucial, real-time information about the dynamic evolution of brain lesion, allowing to avoid secondary injury, recognize adverse events, and improve individualized management of severe acute neurological patients admitted to Neurocritical Care Units (NCCU) [1].

Basic neuromonitoring

Intracranial pressure, cerebral perfusion pressure, and autoregulation

Intracranial pressure (ICP) is derived from cerebral blood flow (CBF) and cerebrospinal fluid (CSF) circulation within the stiff skull [2]. The most reliable methods of ICP monitoring are ventricular catheters and intraparenchymal probes. An intraventricular drain connected to an external pressure transducer is still considered to be a "golden standard" method of measure global ICP. Ventricular catheters allow recalibration and therapeutic drainage of CSF but have significant complications, including hemorrhage, occlusion and infection. Intraparenchymal fiberoptic or microtransducer probes have a minimal associated risk of complications, but can be calibrated only before insertion although the sensitivity drift over time is very small. Critical values of ICP may vary between individual patients but current consensus is to treat ICP exceeding the 20 mmHg threshold [3].

International guidelines for traumatic brain injury (TBI) recommend that ICP should be monitored in patients with Glasgow Coma Scale (GCS) score <8, with an abnormal head CT scan; or patients with GCS score <8 with a normal head CT scan if two or more of the following characteristics are present: age over 40 years, systolic blood pressure <90 mmHg or motor posturing [4, 5]. Recently, Chesnut et al. [6] published the results of the first randomized trial of ICP monitoring in patients with severe TBI. Six months after injury, patient groups had similar scores on functional status and cumulative mortality. For intensivists the strongest clinical implication of this trial is that we need to understand that the true value of ICP is more than a number and should become part of a multimodality approach to targeted therapy [7, 8].

ICP beat-to-beat waveform consists of three components named P1, P2, and P3 that are related to arterial pulse and brain compliance (**Figure 1**). P2 over P1 is a sensitive (99%) but not specific (1-17%) predictor of ICP subsequent increase [9]. Continuous ICP and arterial blood pressure monitoring allow calculation of cerebral perfusion pressure (CPP=ABP-ICP). CPP is the driving force of CBF and the principal determinant of cerebrovascular reactivity to pressure, named cerebral autoregulation. The normal cerebral arterial bed actively reacts to small fluctuations in arterial blood pressure in order to maintain constant CBF over a wide range of CPPs (from approximately 50–150 mmHg). When reactivity is normal the changes in ABP produce an inverse change in cerebral blood volume and hence ICP, but when reactivity is disturbed, changes in ABP are passively transmitted to ICP. Computational methods for continuous assessment of cerebral autoregulation were introduced more than a decade ago and they evaluate dynamic relationships between slow waves of ABP or CPP and ICP or flow velocity [10]. Examples of these methods are moving correlation coefficient, phase shift, or transmission (either in time- or frequency-domain).

The pressure reactivity index (PRx) is calculated as the moving correlation coefficient between 30 consecutive, 10 seconds averaged data points of ICP and ABP [11, 12]. A positive PRx (>0.2) signifies passive reactive vascular bed, while a PRx <0.2 means normal autoregulation. PRx may be used to continuous monitoring of autoregulation and define individual lower limit of autoregulation (LLA) and upper limit of autoregulation (ULA), helping target optimal CPP [13, 14] (**Figure 2**). Retrospective studies show that favorable outcome reaches its peak when CPP is maintained close to optimal CPP [15].

Oxygenation and cerebral blood flow

Brain resuscitation based on basic control of ICP and CPP does not prevent cerebral hypoxia in some patients [16]. Cerebral oxygenation monitoring evaluates the balance between oxygen delivery and consumption [17] and oxygen guided management could lead to improved neurologic outcome [18]. There are several invasive and non-invasive continuous methods of monitoring regional or global brain oxygenation and avoid secondary lesion due to hypoxia (jugular venous bulb oximetry, brain tissue oxygenation, and transcutaneous cerebral oximetry with near infrared spectroscopy).

Brain tissue oxygen pressure

Brain tissue oxygenation pressure (PbtO2) represents the interaction between plasma oxygen tension and CBF [19]. Direct measurement of local PbtO2 with an intraparenchymal probe is becoming the gold standard for oxygen monitoring in NCCU. PbtO2 probes are placed in the white matter and post-insertion head CT confirmation is needed to interpret readings. The normal range is 25-50 mmHg and PbtO2 <15 mmHg is considered the critical threshold for hypoxia [20, 21]. Algorithms of PbtO2-directed therapy should incorporate the management of the several causes of tissue hypoxia (hypoxic, anemic, ischemic, cytopathic, and hypermetabolic) [22] (**Table 1**). Similarly to PRx, the index of tissue oxygen reactivity (ORx), calculated as the correlation coefficient between PbtO2 and CPP, can be

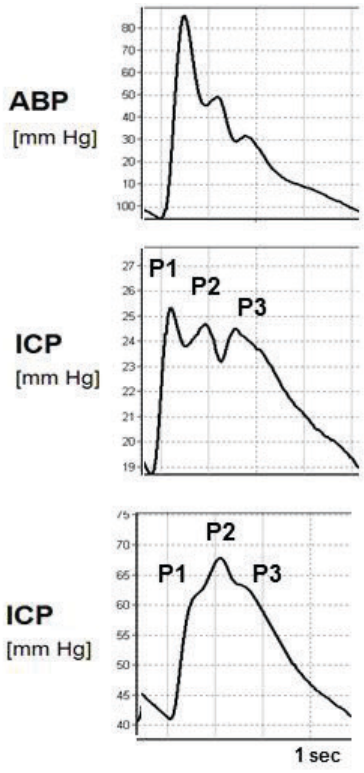

Figure 1. Arterial blood pressure (ABP) and Intracranial Pressure (ICP) waveform. P1 (percussion wave) represents systolic arterial pulsation, P2 (tidal wave) reflects intracranial compliance and P3 (dicrotic wave) represents venous wave that result from closure of aortic valve. In normal conditions, P1 > P2 >P3, but when brain compliance starts to decrease, the amplitude of P2 increases and may exceed P1.

used as an indicator of CBF autoregulation [23]. The concepts of cerebrovascular pressure reactivity and oxygen reactivity are related as high CPP should be avoided if it does not yield improvement in brain tissue oxygenation [24].

Transcranial Doppler and thermal diffusion flowmetry

Continuous direct monitoring of CBF would be helpful to manage acute neurologic patients. Transcranial Doppler ultrasonography (TCD) is a non-invasive method to assess flow velocity as a surrogate of cerebral blood flow. TCD is more frequently used in the diagnosis of vasospasm or hyperemia, but may also be used as a tool to monitor the regulatory reserve of cerebral vasculature to changes in ABP, CO_2, and transient hyperemic response test [25-27]. Thermal diffusion flowmetry (TDF) is based on thermal conductivity and provides a quantitative measurement of regional CBF. Probes are inserted in the white matter, 25 mm below the dura and the normal range is 18-25 ml/100g/min [28]. Continuous monitoring of CBF with TDF and CPP allows calculation of flow-related autoregulation index [29].

Cerebral metabolism and electrical function

Brain metabolism can be assessed by hourly microdyalisis measurement of cell substrates (glucose), metabolites (lactate, pyruvate, glycerol), and neurotransmitters (glutamate) in the extracellular fluid [30]. Normal ranges are described in **Table 2**. Cerebral microdyalisis detects early hypoxia and ischemia and increases the therapeutic window to avoid secondary lesion. However, remains to be established if treatment-related improvement in biochemistry translates into better outcome after acute brain injury [31].

Continuous electroencephalography (cEEG) with or without video surveillance is becoming more widespread in the NCCU [32]. Modern cEEG approaches include quantitative analysis of total power, relative alpha variability and asymmetry detection. The most common indications are: detection of nonconvulsive seizures or status epilepticus, assessment of depth of sedation, detection of ischemia and characterization of clinical signs such as rigidity, tremors, eye deviation, agitation and otherwise unexplained variations of ABP and heart rate [33].

Table 1. Causes of brain tissue hypoxia and management.

Etiology	Pathophysiology	Management of brain tissue hypoxia
Hypoxic	Low PaO_2 Low SaO_2	Lung recruitment and FiO_2 increase Improve O_2 delivery and Hb dissociation curve
Anemic	Low Hb concentration	Red blood cell transfusion
Ischemic	Hypotension, low CPP Hyperventilation Vasospasm Shunt Low cardiac output Dysperfusion	Increase ABP or CPP Increase CO_2 Vasodilation (systemic or local) Treat SIRS or sepsis Improve cardiac output Reduce brain edema
Cytotopathic	Low oxygen extraction Hb high affinity Mitochondrial dysfunction	Improve O_2 delivery Improve Hb dissociation curve
Hypermetabolic	High metabolism	Increase sedation, treat seizures, decrease temperature

ABP = Arterial blood pressure; CPP = Cerebral perfusion pressure; Hb = Hemoglobin

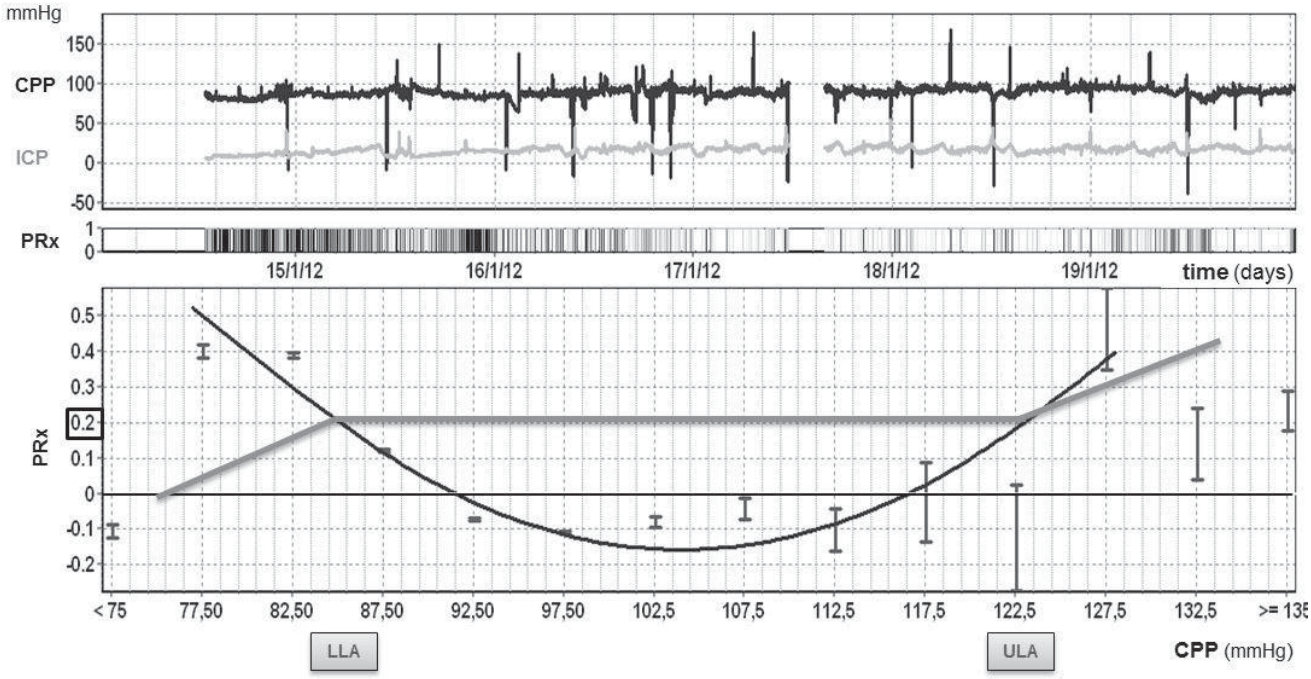

Figure 2. Intracranial pressure (ICP), cerebral perfusion pressure (CPP), and pressure reactivity index (PRx). Continuous monitoring of autoregulation and definition of individual lower limit of autoregulation (LLA) and upper limit of autoregulation (ULA) to target optimal CPP during ICU management.

Conclusion

Multimodal brain monitoring increases the therapeutic window and helps to target treatment avoiding excess or lack of interventions, decreasing cerebral secondary lesions, and systemic complications. Clinical information systems and integrated brain monitoring graphical trends show that pathologic readings precedes clinical deterioration and therefore are an important tool to support proactive medical decision in daily neurocritical care practice.

Abbreviations

ABP: Arterial blood pressure; CBF: Cerebral blood flow; cEEG: Continuous electroencephalography; CSF: Cerebrospinal fluid; CPP: Cerebral perfusion pressure; GCS: Glasgow coma scale; ICP: Intracranial pressure; LLA: Lower limit of autoregulation; NCCU: Neurocritical care units; ORx: Oxygen reactivity index; PbtO2: Brain tissue oxygenation pressure; PRx: Pressure reactivity index; TBI: Traumatic brain injury; TCD: Transcranial Doppler ultrasonography; TDF: Thermal diffusion flowmetry; ULA: Upper limit of autoregulation

Competing interests

The authors declare no conflict of interest.

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Table 2. Cerebral microdialysis normal range of biomarkers and metabolism failure interpretation.

Microdialysis concentration	Normal range	Monitoring interpretation
Glucose	1.5-2.0 mmol/l	Hypoglycemia, cerebral hyperglycolysis Hypoxia, ischemia,
Lactate / Pyruvate ratio	>20-25	Cellular redox state, hypoglicemia Hypoxia, ischemia
Glycerol	>100 µmol/l	Cell membrane degradation Hypoxia, ischemia
Glutamate	>15-20 µmol/l	Excitotoxicity Hypoxia, ischemia

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