SIGNA VITAE 2018; 14(SUPPL 1): 39-41

Methods for detecting and monitoring cerebral vasospasm in aneurysmal subarachnoid hemorrhage

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INTRODUCTION

Critical thinking about diagnostics and monitoring of cerebral vasospasm must take into account few basic facts. The first important thing is to distinguish two anatomically different structures: cerebral blood vessels and living tissue of the brain. Size and shape of cerebral arteries are the main point in radiological (digital subtraction angiography and other) morphological methods of investigation in brain heamodynamics. Changes in living brain tissue during brain ischemia can be detected by biochemical (cerebral microdialysis) or physical methods (magnetic resonance imaging, electrophysiology). Therefore, considering symptomatic cerebral vasospasm, at least two different methods of diagnostics should be applied: morphological one for detecting the size and shapeof cerebral arteries, and biological or physical one for detecting ischemic brain tissue.

The second important fact in diagnostics of cerebral vasospasm is the definition of vasospasm itself. There must be clear clinical scenario (subarachnoid hemorrhage) and clear distinction to other similar pathology (reversible cerebral vasoconstriction syndrome).

These facts make an important logical frame in diagnostics of cerebral vasospasm. Clinically significant and symptomatic vasospasm develops in 20-30% of patients with aneurysmal subarachnoid hemorrhage (SAH). It is a major contributor to higer mortality and permanent disability rate. However, vascular imaging methods show incidence of cerebral vasospasm in up to 40-70% of SAH patients, but not all are symptomatic (1).

Symptomatic vasospasm is defined as the presence of neurological worsening including focal deficit, decline in level of consciousness, and motor paresis; no other identifiable cause (intracranial disorder and systemic complication) of neurological worsening; and confirmation of vasospasm by medical examinations (1-3).

Delayed cerebral ischemia (DCI) is a broader term that refers to the delayed development of a focal neurological deficit, decline in level of consciousness and/or cerebral infarction. It includes a number of clinical entities, one being symptomatic vasospasm. Exact mechanisms responsible for development of vasospasm and delayed cerebral ischemia are still unknown. Possible candidates are recognized as factors in pathophysiology of vasospasm (nitrous oxide, endothelin, oxyhaemoglobin, thrombin, serotonin, thromboxane A2, noradrenaline, sphingosine-1-phosphate), but further research is needed. Some patients develop delayed ischemic neurological deficit without angiographyc cerebral vasospasm. Recent studies suggest that vasospasm isn't the only contributor for developing delayed cerebral ischemia and that pathophysiology is probably multifactorial.

Diagnosing symptomatic vasospasm is difficult, especially in sedated or comatose patients. It is made by exclusion of all other causes of neurological deficit or conciousness level deterioration. The ideal diagnostic method for detecting cerebral vasospasm should be fast and easy to perform bedside, easily reproducible, with a high specificity and sensitivity, without any adverse effects or complications, and cost-effective. In this paper we will focus on available methods of diagnosing and monitoring of cerebral vasospasm.

METHODS OF MONITORING CEREBRAL VASOSPASM

Digital subtraction angiography

Digital subtraction angiography (DSA) of cerebral arteries is the gold standard of diagnosis of cerebral vasospasm. It is highly sensitive and specific in detecting cerebral vasospasm. Nevertheless, it is an invasive procedure, requires substantial amount of resources, patient needs to be sedated and it is time consuming. DSA is associated with <1% risk of complications, major ones being dissection of artery or intraarterial thrombosis. One study reported a 2.6% risk of a second hemorrhage from a ruptured aneurysm during DSA performed within 6 h after initial SAH. During DSA procedure, the distal intracarotid pressure rises during injection of contrast medium, which could potentially lead to re-rupture of an aneurysm. DSA can be utilized to apply vasodilatating agent selectively to the affected artery or provide access to endovascular intervention such as balloon angioplasty. Major limitation is difficulty in inspecting distal parts of cerebral arterial tree (2).

CT Angiography

CT Angiography (CTA) is considered to be less invasive than DSA, highly sensitive and specific method with the procedure lasting significantly less, and is associated with a lower risk of re-rupture (4). Compared to DSA it is accurate in detecting cerebral vasospasm in proximal, higher-lumen arteries but is less accurate in mild to moderate vasospasm in distal arteries (5).

Contrast media containing iodine used either for DSA or CTA can have direct spastic effect by hyperosmolarity and also by stimulation of vasomotor mediators, promoting vasoconstriction (6). Quality of CTA imaging is affected by the patients' movement or artefacts after coiling or clipping of an aneurysm, superposition of vascular structures other than those in focus of examination. Both CTA and DSA have been shown to overestimate the severity of vasospasm.

Low-dose perfusion computed tomography

Low-dose perfusion computed tomography (CTP) is non invasive method to diagnose cerebral vasospasm with high specificity and sensitivity. A decrease in cerebral blood flow (CBF) and prolongation of mean transit time (MTT) on baseline CTP performed within 3 days following SAH have been found to be >90% specific for the development of vasospasm (7). Reports also show that CTP can be a method to predict delayed cerebral ischemia and can give prognostic information in SAH patients (8).

Transcranial Doppler ultrasonography

Transcranial Doppler ultrasonography (TCD) is an ultrasound method of detection of high speed blood flow through cerebral arteries. This method is non-invasive, inexpensive, fast, easily reproducible and repeatable during the course of treatment. It has no serious side effects and can be done real-time along patients bedside. It depends on the experience of the person performing the procedure. Another disadvantage of TCD is its inability to detect vasospasm in smaller blood vessels, in vessels positioned deeper in the brain tissue and those covered with thicker bone, such as posterior circulation arteries. Even in examining middle cerebral artery up to 20% of patients have inadequate ultrasound window through temporal bone (9). TCD is based on a principle that a decrease in a diameter of a vessel will cause an increase in a blood flow velocity, but there are many other factors influencing cerebral blood flow and mean velocity flow. These factors include age, sex, hypercarbia, hematocrit level, mean arterial pressure and pregnancy (10).

Meta-analysis testing reliability of TCD to predict proximal middle cerebral artery spasm, found prediction rate of 97%, but sensitivity of this method of only 67% (11). Results on sensitivity and specificity in evaluating anterior cerebral artery and posterior cerebral artery are poorer. Combining various ratios such as Lindegaard ratio (middle cerebral artery flow velocity/internal carotid artery flow velocity) or spasm index (TCD velocity/hemispheric CBF) signifficantly improved sensitivity of TCD. There are no relevant data that TCD-guided therapy and decision-making based on TCD findings influence outcome of patients with anurysmal SAH. Despite all limitations, Neurocritical Care Society in its recommendations still names TCD as a tool for monitoring and detection of large artery vasospasm with variable sensitivity. Recommended thresholds of mean blood flow velocities are <120 cm/s for absence and >200 cm/s and/or MCA/ICA ratio >6 for presence of vasospasm (12).

Magnetic resonance imaging

Perfusion-weighted magnetic resonance imaging (MRI) can detect small areas of early ischemic injury and locate the vasospasm. With this method it is possible to calculate cerebral blood volume and by combining it with mean transit time, patients who may benefit from hemodynamic augmentation therapy can be differentiated (13). Diagnostic procedures such as positron emission tomography (PET), xenon-enhanced CT (Xe-CT), and single-photon emission computed tomography (SPECT) can detect areas of reduced metabolism and higher oxygen demand, but just like MRI, can not pin-point the causative vessel.

Brain tissue oxygen monitoring

Brain tissue oxygen monitoring is a diagnostic method in which the catheter is inserted in the penumbra (potentially salvageable brain tissue surrounding ischemic core). It continuously collects data such as brain tissue oxygenation, partial pressure of oxygen and carbon dioxide, pH and temperature. Studies show correlation between tissue oxygen pressure (PtiO2) and vasospasm. Loss of autoregulation in the affected parts of the brain can be seen using this type of monitoring, by correlating the PtiO2 to the MAP (14,15).

Based on information collected by the catheter, haemodynamic support is used to elevate cerebral blood flow and/or oxygen delivery, improve carbon-dioxide washout, and sedation is sometimes used to reduce metabolic rate of oxygen. It is possible to determine the effect of any therapeutic intervention in real time. Randomized controlled studies about influence of guiding therapy according to PtiO2 values on outcome of SAH patients are lacking. Major limitation of this method is invasiveness and correct positioning of probe.

Cerebral microdialysis

Cerebral microdialysis is an invasive diagnostic procedure that can evaluate focal levels of various metabolic substrates (such as glucose, glutamate, lactate, but there is a variety of other ones that can be measured). Rise of anaerobic metabolite levels is specific for cerebral ischaemia and can even be used as a prognostic tool in delayed ischaemic injury (16).

Jugular venous bulb oximetry

Jugular venous bulb oximetry can provide data about the global cerebral blood flow, cerebral oxygen demand, oxygen delivery, lactate production and pH mostly from ipsilateral brain hemisphere. Samples can be taken intermitently or oxygen saturation in the jugular venous bulb can be continuously monitored. Very brief and transient episodes of cerebral desaturation, even for as long as 15 minute, can be a sole prediction factor of poorer neurological outcome (17). It can also be used to monitor the effect of therapeutic interventions (18). Investigation on small group of patients show that increase in cerebral oxygen extraction is predictive for symptomatic vasospasm (19). It is an invasive method with risk of developing thrombus at the catheter tip or other complications related to the procedure of placing the catheter (haematoma formation, bacteriemia and infection, arterial puncture). Monitored parameters are from pooled blood, so it is possible that normal surrounding areas may mask a local change, thus reducing the sensitivity of jugular bulb venous oximetry.

Near infrared spectroscopy

Near infrared spectroscopy (NIRS) is noninvasive diagnostic method used to evaluate tissue oxygenation by emitting near-infrared light through the skull and into the cerebral cortex near the surface. Reflected light is then converted to the electrical signal similar to that of the pulse oxymetry, giving quantitative information about oxygen saturation. It can be used continuously. Measurement of cortical oxygen saturation can give information on regional cortical blood flow, and can also be used to assess autoregulation and vasospasm. One study on a small group of patients concluded that NIRS is a comparable method with CT perfusion imaging and may serve as a noninvasive, safe, bedside monitoring tool for regional brain oxygenation and indirectly cerebral blood flow. Another recent report found cortical oxygen saturation decrease to be predictive for vasospasm of middle cerebral artery (20,21). There are several other papers confirming these findings, but larger prospective studies are needed in order to validate this method before it becomes a standard practice of care for SAH patients.

Other neuromonitoring devices

There are numerous haemodynamic monitoring devices and methods used today, but as the technology advances, many more are being developed to be more efficient, safer, faster and easier to use. One of the new devices currently is NAS-1000, the haemodynamics neuromonitor which detects neurovascular pulsatility waveforms. It is noninvasive and apropriate for continuous use. Low frequency acoustic signal is being detected and converted to a waveform pattern that, depending on the amplitude and frequency, can detect neurovascular pathology. In one prospective, non-randomised study that included

athletes suffering from concussion, NAS-1000 detected concussion with a sensitivity of 86.1%, and specificity of 91%, and these numbers tell us of it's potential in predicting this clinical entity (22). Since the FDA approval is still pending, there are studies to be made to prove its sensitivity and specificity to different conditions that affect cerebral haemodynamics. Optoacoustic imaging is promising developing technology that combines anatomic and functional imaging in real time and can successfully detect cerebral hemodynamic changes associated with brain function (23).

To conclude, there are many neuromonitoring devices and techniques used today, giving valuable information mainly about cerebral haemodynamics. These methods are being constantly improved and new approaches to monitoring CBF, CBV, glucose utilization and cerebral oxygenation are being investigated and put into everyday practice in neurosurgical critical care units. Even though the use of cerebral haemodynamics monitoring is imperative in the neurosurgical ICU, the best approach to assess perfusion and metabolism of the brain seems to be the combination of different methods, intermittently or continuously collecting information. It is important to recognize indications and familiarize with old as well as new methods to provide best possible treatment and to be able to employ individually tailored therapy for each patient.

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