Hemodynamic physiology during perioperative intracranial hypertension

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Essential cerebral physiology and technical background
Cerebral Blood Flow

The brain is unique in that it is supplied by four major arteries that join in an equalizing manifold, the circle of Willis. The carotid arteries each supply approximately 40 percent of the total perfusion requirements of the brain. Four major, interdependent mechanisms are involved in the control of cerebral blood flow:

1. Metabolic coupling
2. Neural control
3. PaCO₂
4. Autoregulation.

Metabolic Coupling
The adult human brain represents about 2% of total-body weight, but in normal circumstances receives 12 to 15% of cardiac output. This reflects the brain’s high metabolic rate and oxygen consumption. This metabolic rate is highly dependent on local brain activity, and there are elaborate mechanisms for the regulation of the cerebral blood flow (CBF). Neuronal activity is the principal energy-consuming process in the brain. Local cerebral blood flow adjusts to the level of energy generation. Normally there is exquisite coupling between the regional cerebral metabolic demand for oxygen and glucose generated by local neuronal activity and the volume of blood flowing through that tissue. Local blood flow increases as soon as 1 s after neuronal excitation and the zone of increase is limited to 250 µm around the site of the increased activity¹. This indicates that flow can be adjusted very rapidly at the microvascular level according to metabolic demands in discrete functional subunits. This phenomenon is called metabolic coupling. Nonetheless, in many clinical conditions, the CBF may increase or decrease out of proportion to metabolic demands.

Neurogenic Control
The perivascular innervations - a dense plexus of nerve fibers in the walls of cerebral vessels - of the cerebral blood supply form an additional coupling mechanism between metabolism and flow. These consist of sympathetic and parasympathetic fibers and have an important role in the tonic control of the cerebral blood flow.

Carbon Dioxide Tension (PaCO₂)
Alterations in PaCO₂ result in marked vasodilation. There is an exponential relationship between PaCO₂ and CBF within a PaCO₂ range of 25 to 60 mmHg, with a CBF change of approximately 4 percent per mmHg. Flow changes induced by alterations in PaCO₂ occur within 2 min and reach a new plateau within 12 min. This regulatory mechanism is a function of changes in the perivascular pH in the vicinity of the vascular smooth muscle cells, rather than a direct effect of CO₂ per se. Prolonged alterations in PaCO₂ result in chronic
adaptation, and after approximately 36 h the blood flow changes tend to return to prealteration levels.

In conscious patients, fast changes in PaCO\textsubscript{2} are avoided by homeostatic mechanisms. However, during surgical conditions important alterations in PaCO\textsubscript{2} may occur. This can result in several undesired effects. Firstly, unnecessary increased CBF induces cerebral swelling and consequently increased ICP. Secondly, increased CBF in healthy regions may redirect bloodflow from at-risk regions, thereby causing an intracerebral steal phenomenon. Severely decreased CBF can induce cerebral tissue ischemia. Therefore, maintaining normocapnia is essential to preserve cerebral haemodynamic homeostasis.

**Autoregulation**

The cerebral autoregulation refers to the capacity of the cerebral circulation to adjust its resistance so that it can maintain CBF constant over a wide range of mean arterial pressure (MAP) values. The lower limit of autoregulation has been widely quoted as a MAP of 50 mmHg, although there is considerable interindividual variation. Above and below the autoregulatory plateau, the CBF is pressure dependent and varies linearly with the MAP. It is important to stress that both the upper and the lower limits of autoregulation can be affected by many factors, including sympathetic nerve activity, Pa\textsubscript{CO\textsubscript{2}} and pharmacologic agents. The most important factor that can affect autoregulation is chronic arterial hypertension. As a result of thickening of the cerebral arteries, the upper and lower limits of autoregulation are both displaced to higher levels in patients with chronic hypertension. The consequence of these alterations is that symptoms of cerebral hypoperfusion can occur at higher values of mean arterial pressure in patients with chronic hypertension than in normotensive individuals.

**Cerebral Blood Flow and Ischemic Thresholds**

The brain is one of the most metabolically active organs in the body and is exquisitely sensitive to hypoperfusion and hypotension. Its high metabolic demand and lack of appreciable energy reserves render the central nervous system uniquely susceptible to alterations of blood supply. Severe reductions in CBF (<10ml/100g/min) lead to rapid neuronal death. 10 seconds after cessation of CBF, unconsciousness develops. Irreversible damage occurs within minutes.
*Intracranial Pressure (ICP)*

The brain is enclosed in the cranium, which has a fixed volume; therefore, if any of the components located in the cranial vault increase in volume, the ICP will increase. This can result in reduced blood flow to the brain\(^2\). The ICP is normally less than 10 mmHg. Under normal circumstances, a small increase in intracranial volume will not greatly increase ICP because of the elastance of the components located in the cranium: brain(80%), blood(12%) and CSF(8%). After a certain point, however, the capacity of the system to adjust to increased volume is exceeded and even a small increase in volume will increase ICP\(^3\). This principle is generally known as the Monro-Kellie hypothesis\(^4\).

*Cerebral Perfusion Pressure (CPP)*

In cases of substantially increased ICP or increased Central Venous Pressure (CVP), this becomes of foremost importance, because the cerebral perfusion is more precisely determined by the CPP (CPP = MAP − ICP or CPP = MAP − CVP).

*The Cushing Reflex*

Harvey Cushing was the first to describe, based on his clinical experience as a neurosurgeon, a triade of hypertension, bradycardia and apnea as a result of intracranial hypertension\(^5\). Heymans showed in animal research that there is an initial short-lasting tachycardia before the onset of bradycardia\(^6\), but it is only since the introduction of neuro-endoscopy, this has become of clinical relevance. Relying on the experience in relatively slow-evolving processes like subdural haematoma, hydrocephalus or cerebral tumors, many clinicians still consider bradycardia and hypertension as the first haemodynamic sign of intracranial hypertension. In our research, we clearly demonstrate that the initial signs of hyperacute intracranial hypertension – as commonly seen during endoscopic neurosurgery – consists of a combination of hypertension and tachycardia.
The Ventricular system

Meninges
The brain and spinal cord are covered and protected by three layers of tissue called meninges. From the outermost layer inward they are:

1. The dura mater: a strong, thick membrane that closely lines the inside of the skull.
2. The arachnoid mater: a thin, web-like membrane that covers the entire brain.
3. The pia mater hugs the surface of the brain and has many blood vessels that reach deep into the brain.

The space between the arachnoid and pia is the subarachnoid space. It is here where the cerebrospinal fluid bathes and cushions the brain.

Ventricles
The lateral ventricles are located bilaterally deep within the cerebral hemispheres. They both connect with the third ventricle through the foramen of Monro.

The third ventricle connects with the fourth ventricle through the aqueduct of Sylvius, a long narrow tube.

The fourth ventricle is connected with the subarachnoid space.
Cerebrospinal fluid

The cerebrospinal fluid (CSF) is a clear colorless fluid that surrounds the brain and fills the ventricular system. This circulating fluid is constantly being absorbed and replenished.

The choroid plexus, a vascularised structure that is located in the brain ventricles, produces CSF at about a rate of 500 ml/day. The CSF circulates from the lateral ventricles into the third ventricle, then by passing the cerebral aqueduct, to the fourth ventricle and into the subarachnoid space which surrounds the brain and the spinal cord. In the subarachnoid space, the CSF is absorbed through specialized cell clusters, the arachnoid villi near the top and midline of the brain. The arachnoid membrane permits the uni-directional flow of CSF out into the venous blood.

The CSF has many different functions: the mechanical protection of the brain, the regulation of the intracranial pressure, keeping the brain tissue moist and finally the distribution of metabolites.

A balance is maintained between the amount of CSF that is absorbed and the amount that is produced. A disruption or blockage in the system can cause a build up of CSF, which can cause enlargement of the ventricles (hydrocephalus) or cause a collection of fluid in the spinal cord (syringomyelia).
Blood supply

Blood is carried to the brain by two paired arteries, the internal carotid arteries and the vertebral arteries. The internal carotid arteries supply most of the cerebrum. The vertebral arteries supply the cerebellum, brainstem, and the underside of the cerebrum. After passing through the skull, the right and left vertebral arteries join together to form the basilar artery. The basilar artery and the internal carotid arteries “communicate” with each other at the base of the brain called the Circle of Willis. This communicating system is an important safety feature of the brain. If one of the major vessels becomes blocked, it is possible for collateral blood flow to come across the Circle of Willis and prevent brain damage.

The venous circulation of the brain is very different than the rest of the body. Usually arteries and veins run together as they supply and drain specific areas of the body. However, this is not the case in the brain. The major vein collectors are integrated into the dura to form venous sinuses. These collect the blood from the brain and pass it to the internal jugular veins. All sinuses eventually drain to the sigmoid sinuses, which exit the skull and form the jugular veins.
Transcranial Doppler

Transcranial Doppler assessment of the cerebral blood flow velocity is based on the Doppler effect, first described by Christian Doppler in 1842. Its use as an imaging device is based on the observation that the frequency of an ultrasound wave reflecting from moving erythrocytes changes proportional with the velocity of the blood flow. Hence, the blood flow velocity can be deduced from the change in frequency between emitted and reflected ultrasound waves. Two important limitations arise in the implementation of this principle in medical imaging. Firstly, the ultrasound beam should be as parallel to the blood flow as possible. Secondly, Attenuation of the ultrasonic wave near the skull resulted in barely reproducible reflections, making adequate recordings of blood flow velocities from intracranial arteries almost impossible. As a result, its use to examine cerebral blood flow was only possible since 1982, after introduction of a high-energy bidirectional pulsed Doppler system operating at frequencies of 1-2MHz. As a result of these two limitations, Doppler measurements of cerebral arteries is limited to certain ‘acoustic windows’ in the skull. In this research, the temporal acoustic window was used to insonate the middle cerebral artery.

Transcranial oximetry

Near-Infrared spectroscopy (NIRS) is a noninvasive optical method for monitoring cerebral regional oxygenation. It is based on the principle that light in the near-infrared range (700-900 nm) readily penetrates skin and bone, but reflects off certain chromophores in the brain, such as oxy- and deoxyhaemoglobin and cytochromes AA. Therefore, by monitoring the absorption of light at several wavelengths in near-infrared range, brain haemoglobin oxygen saturation can be measured. The NIRS device used in this research uses laser light at four precise wavelengths to capture information needed for the algorithm to calculate the absolute value of the mixed cerebral haemoglobin oxygen saturation (SctO2). SctO2 is defined as the ratio of concentrations of HbO2 to Hb + HbO2 in the brain tissue. The value of SctO2 reflects a proportional mix of arterial and venous blood. It is estimated that the NIRS cerebral oximeter interrogated brain tissue microvasculature is approximately 70% venous and 30% arterial during most physiological conditions.
Endoscopic Neurosurgery

Neuro-endoscopy involves passing a tiny viewing scope into the ventricles. The neurosurgeon thus has a clear view of the inside ventricular system. For several intracranial pathologies, the obvious advantage of an endoscopic approach is minimal disturbance of brain tissue and consequently less postoperative morbidity. In most cases, the classical entry point is at 2 cm lateral from the midline (in order not to damage the corpus callosum and the Pericallosal blood vessels) and anterior of the coronary suture. Then the endoscope enters the lateral ventricle, and is further advanced through the ventricular system, depending on the location of intervention. A frequent intervention to treat some forms of hydrocephalus is a third ventriculostomy, where a perforation is made of the floor of the third ventricle in an attempt to bypass an obstruction of the aqueduct of Sylvius\(^\text{12}\). During this procedure, rinsing of the ventricular cavities is required, which often induces severe intracranial hypertension.

Computerised analysis of physiological data

In order to elucidate the exact sequence of haemodynamic events during hyperacute intracranial hypertension, intensive computation of the data was essential. Therefore, I needed to develop custom-made software to synchronize, compute and analyse the megabytes of specific waveform data of each patient. These algorithms were written in Visual Basic language and visualised in Microsoft Excel. In the successive research projects, different algorithms were developed to determine the computed parameters of interest.
References

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