Anaesthesia Update

Vol. 13 No.1

Editorial Office

Anaesthesia House, Panampilly Nagar
Cochin 682 036, Kerala, India
Phone: 0484-4010551, 2322251
Email: isacochin@gmail.com

For Private Circulation only

Annual Subscription of Anaesthesia Update is Rs.100/-.
For copies send DD drawn in favour of ISA Cochin City Branch, payable at Cochin, to the Editorial Office.

Anaesthesia Update

Vol. 13 No.1

CONTENTS

designed & produced by pixel studio, cochin-28 ph : 2806301

From the President's Desk

Dear ISA members,

Warm Greetings.

Congratulations to the Editorial Board for the fruitful works that you have rendered to make this *Update* march ahead of its times. The new informative sections of this issue on Neuro-anaesthesia will definitely increase its readership. May this issue stimulate the future issues to have more pages to accommodate more contributors and thus serve to be a beacon of light and radiance of our branch of Anaesthesiology.

I wish this issue all success.

With best wishes and warm regards ,

Dr. Austin Pius
President
ISA Kerala State Branch

From the Secretary's Desk

Dear friends,

The first issue of our journal *Anaesthesia Update* is in your hand now. Though our term started early, the journal comes a bit late as our editor left for Doha on employment. However, Dr. Jiju John alongwith our former editor Dr. Abraham Cherian and associate editor Dr. Kurien P. Thomas has brought out this issue in a nice way.

The period so far was very good in terms of association activity. Our own Dr. B. Radhakrishnan is elected to the post of national president of our organization, a lifetime achievement anyone can have in his association activity; an honor to Kerala, proud to all of us.

For the first time we have observed anesthesia day as a state level function at Calicut. We had three GC meetings and a special meeting of constitution committee to finalize the draft constitution for circulation. Association and academic activities are being conducted in a good way in almost all the city branches. Our president Dr. Austin Pius has visited most of the city branches. Many city branches have organized receptions for Dr. B. Radhakrishnan, our national president.

A dreaded development in this period is starting of short-term course (12-18 weeks) in obstetric anaesthesia for MBBS graduates at designated medical colleges to cater the need of rural India, a plan of H & FW department of the government of India. The course has started in a few states. We all must unite and oppose this short-term course as it is too short even to learn resuscitation. If the govt. is really concerned about the health of rural people, let it produce qualified anaesthesiologists by increasing the seats for D.A. in medical colleges to fill the gap and relocate the anaesthesiologists in service who are posted elsewhere. Let the govt. make the working condition and remuneration of anesthesiologists in service attractive or make it par with that of their colleagues in private sector and our govt. will get qualified anaesthesiologists. Let us not allow the govt. to differentiate between the rural and urban people in anaesthesia services.

The state annual conference is at Thiruvalla during the 2nd week of October and national conference at Mysore during the week of December. Register for both of them in large numbers and attend the academic and association activities.

Long Live ISA,
Yours sincerely,

Kasaragod — **Dr. Venkatagiri K.M.**
04.05.2006 — Hon. Secretary

Editorial

We have great pleasure to present you the first issue of "Anaestheisa Update" for the Year 2006.This issue deals with various interesting topics in Neuro Anaesthesia. Neuro Anaesthesia has evolved into a major subspecialty of Anaesthesiology over the years and we are encountering a large number of Neuro surgical procedures in our daily clinical practice. The various authors have taken great efforts to cover extensively the various aspects of Neuro Anaesthesia. The editorial board expresses its sincere thanks and gratitude to the various distinguished authors for their valuable contributions. We hope this issue will help us to gain a clear understanding of the various concepts and strategies in neuro anaesthesia.

We are also thankful to the industry for the support they have been rendering towards the publication of this issue.

Dr. Jiju John

Cerebral Protection

Dr. P.R. Suneel

Discussion of cerebral protection cannot be complete without an initial understanding of the normal ionic mechanisms at work in the neurons and their alteration during cerebral ischemia. Though much progress has been made in elucidating the ischemic cascade, the progress on the neuropharmacologic front has been disappointing

BASIC PHYSIOLOGY AND PATHOPHYSIOLOGY

Ion homeostasis[1]: Sodium and potassium concentrations across the neuronal cell membrane are tightly maintained such that the intracellular potassium is high and intracellular sodium and calcium is low. These concentration gradients are maintained by energy consuming ion channels such that the inside of the cell is negative compared to the outside. Depolarization of the neuron produces passive diffusion of Na down its concentration gradient into the cell. Repolarization is characterized by active extrusion of Na outside the cell with reaccumilation of K inside the cell. Of more interest is the role of calcium, an important 'second messenger'. The intracytoplasmic calcium is kept low by energy dependent processes that act either by extrusion of calcium outside the cell in exchange for Na^+ or the calcium ions are pushed into the endoplasmic reticulum or the mitochondria. During ischemia, when these energy dependent processes are inactivated, calcium begins to accumulate in the cell. The normal intracellular pH of the neural cell is 6.94-7.06. Hydrogen ion inside the cell is generated by metabolic processes and also by passive diffusion from extracellular compartment. This H^+ is neutralized or consumed either intracellularly or pumped out by energy requiring processes.

Brain Metabolism: Energy requirements of neurons may be broadly classified as subserving two components.

a) Energy required for neuronal function or activation metabolism. This refers to the energy that is required for generating electrical activity and is spent on maintaining Na-K homeostasis after depolarization. It constitutes about 55% of the total energy demands.

* *Assistant Professor, Dept. of Anaesthesiology, SCTIMST, Trivandrum*

b) Residual metabolism: Refers to the energy needed for membrane stabilization, i.e. ion pumping to maintain ion concentration gradients across the cell membrane, synthesis and handling of neurotransmitters etc. Residual metabolism persists even after an isoelectric EEG is achieved. This constitutes 40-45% of total energy requirements.

Flow thresholds[1, 2]: CBF is relatively constant over a broad range of blood pressures between a mean arterial pressure (MAP) of 60-150 mm Hg i.e. the cerebral autoregulation. Below a MAP of 60 mmHg, autoregulation fails and CBF decreases. Ischemic flow thresholds refer to the level of blood flow at which energy requiring functions of the cell fails. This depends not only on cerebral blood flow (CBF) but also on the functional state of the neuron.

a) The upper ischemic flow threshold is that flow at which normal or electrical activity ceases. At this flow, brain will attempt to overcome ischemia by increasing oxygen extraction. Eventually, brain may become electrically quiescent but cellular integrity is maintained. If blood flow is re-established, then full recovery of neuronal function occurs.

b) The lower ischemic flow threshold is that flow at which there is ATP depletion causing membrane and mitochondrial failure. It is associated with cell death.

Between these two ischemic thresholds, small increase or decrease in CBF can make the difference between neuronal recovery and irreversible damage. Normal CBF in healthy volunteers has been measured at 50ml/min/100 gm of brain tissue. EEG signs of cerebral ischemia occur at 25ml/min/100gm. Under conditions of neurolepta-nesthesia cerebral ischemia does not occur upto 15-18ml/min/100 gm and under isoflurane nitrous oxide anesthesia ischemia is tolerated to a level of 8-10 ml/min/100 gm. From animal studies, it is known that membrane failure occurs at 6-8 ml/min/100 gm.

Cerebral metabolism[1, 3]: Brain depends on glucose as the sole source of its energy. Glucose is subjected to two metabolic pathways in the neurons, the Embden-Mayerhof pathway (EMP) in the neuronal cytoplasm, which can take place even in the absence of oxygen and the tri-carboxylic acid cycle (TCA) in the mitochondria, which can take place only under aerobic conditions. EMP generates two molecules of adenosine-tri-phosphate (ATP) and pyruvate. Pyruvate is then subjected to the TCA cycle, such that a single molecule of glucose produces 38 molecules of ATP. Brain has low stores of these high-energy phosphate compounds, no oxygen stores and minimal glucose

stores. Therefore it is very dependent on circulation for substrate delivery for energy requirements. If oxygen is not available, mitochondria can neither metabolize pyruvate nor neutralize the H^+ generated. Anaerobic glycolysis, then takes over. In this process one molecule of glucose yields only two molecules of ATP and pyruvate is converted to lactic acid. This process produces H^+, which will cause fall in intracellular pH and worsen cell damage in the presence of continuing ischemia. Anaerobic process generates insufficient amounts of ATP and in the presence of on going ischemia the availability of glucose also falls.

Cellular processes that require energy: Most of the energy requirements are for maintaining ion pumps that work in maintaining large electrochemical gradients across the cell membrane. Neuronal activity causes large-scale movements of ions and the ion pumps require even more energy. When ATP becomes unavailable the neurons become unexcitable initially and later become irreversibly damaged. Neurons also require energy to maintain their structural and functional integrity. The cell membranes, internal organelles and cytoplasm are made of carbohydrates, lipids and proteins that require energy for their synthesis. Ion channels, enzymes and structural components are protein molecules that are continuously synthesized and degraded in normal functional neurons. This is another source of energy consumption.

Cerebral ischemia: Cerebral ischemia results when a decrease in tissue perfusion exceeds the tissues ability to increase oxygen extraction from the blood and consists of inadequate oxygen delivery, inadequate CO_2 removal, increased intracellular lactate production and decreased ATP.

Ischemia may be global or focal. Global ischemia occurs with cardiac arrest and results in cessation of oxidative phosphorylation within 15-20 seconds. Anaerobic metabolism will breakdown the available glucose stores until they are depleted. Lactic acid, the by-product in this process, will cause a decrease in intracellular pH. Once glucose stores are exhausted, ischemic cascade is set in motion, which will ultimately result in cell death.

Focal ischemia, results from interruption of blood flow through a single arterial distribution. The residual CBF depends on collateral circulation and perfusion pressure. Flow through the collateral channel creates a topographic gradient, from a central core of irreversible infarction to surrounding normal brain, which also includes an area of functionally silent, but viable tissue, the ischemic penumbra. The potential for neuronal recovery in ischemic penumbra is great. But in the presence of continuing ischemia, the penumbral tissues gradually degenerates and progresses to infarction unless salvaged by reperfusion. Thus both the depth and duration of ischemia are important factors in determining the outcome of ischemia.

Secondary consequences of ischemia: Damage continues to occur during the reperfusion phase of ischemia. This is called post-ischemic or reperfusion injury. This includes extracellular events such as tissue edema, vasospasm and red cell sludging all of which can produce post-ischemic hypo-perfusion. Intracellular events such as acidosis, release of glutamate, increased metabolism and increased calcium load, free radical generation and membrane damage further worsens cerebral injury. It is clearly of advantage if drugs can block this phase of ischemic injury even if the primary event that led to cerebral ischemia cannot be prevented. Secondary vascular changes:

a) No re-flow phenomenon: increased viscosity of stagnant blood and compression of microcirculation by tissue edema may lead to no-reflow phenomenon.

b) Reactive hyperemia: When blood flow is re-established following ischemia, there is a brief period when the blood flow is high. This may be due to the low viscosity of blood washing in compared to the stagnant blood in the ischemic area or due to increase in local metabolism.

c) Post-ischemic hypoperfusion: Occurs after the hyperemic phase and may last between 6-24 hours. This may contribute to ultimate neurological damage. Hypoperfusion may be due to vasoconstriction, which can be a result of calcium influx or production of eicosanoids. Extrinsic mechanical compression may also be another reason.

Ischemic cascade[2]: The central event precipitated by cessation of blood flow to the neurons is cessation of oxidative phosphorylation. During ischemia both the supply of glucose and the washout of metabolites is inhibited. The activities of ATP dependent ion pumps are reduced, intracellular levels of Na and Ca increases and that of K falls. This causes the neurons to depolarize and release excitatory amino acids such as glutamate. High levels of glutamate further depolarize the neurons by activating amino-3-hydroxy-5 methyl-4-isoxazole (AMPA) and n-methyl-d-aspartate (NMDA) receptors, further increasing Na and K conductance and Ca influx. Glutamate also releases Ca from its intracellular stores. This damage wrecked by glutamate is called excitotoxicity. Loss of tightly regulated calcium

homeostasis leads to activation of a number of enzymatic pathways that lead to further damage. Protein kinases alter neuronal homeostasis by phosphorylating key proteins in metabolic pathways. Examples of such proteins are calpain, which causes cytoskeletal proteolysis, endonucleases that lead to DNA fragmentation, and lipases, which cause production of arachidonic acid metabolites and lead to the formation of free radicals. The net effect is widespread disruption of cytoskeletal integrity and damage to mitochondrial function.

MONITORING CEREBRAL ISCHEMIA:

Intracranial pressure (ICP) monitors [1,4]: A Glasgow coma scale of 8 or less warrants the use of an ICP monitor. Intraventricular catheter introduced by Lundberg in 1960 continues to be the gold standard for ICP monitoring in the absence of bleeding disorders. The advantage with this type of device is that CSF drainage can be accomplished. Disadvantage includes, higher chances of infection and potential to cause brain injury during placement. Fiberoptic ICP monitoring devices are available that reduce the chance of infection but significant disadvantages includes, difficulty with calibration, drift, expense and fragility of device. Besides these monitors should be replaced every five days. ICP monitors that use microchip pressure transducers and not fiberoptic cables have also been used and found useful.

The normal ICP waveform consists of small pulsations, which correspond to systolic arterial pressure waves and 'a' wave of CVP. Normal ICP increases during inspiration on mechanical ventilation. When ICP increases to 20-30 mm Hg it looses its venous pulsations and assumes an arterialized shape. Of ominous significance are the so-called Lundberg A waves or plateau wave. They are abrupt in appearance with amplitude of 50-100 mmHg above baseline. It usually signifies severe intracranial hypertension and that spatial exhaustion has occurred. If not aggressively treated, death will ensue.

Transcranial Doppler (TCD): Inexpensive, noninvasive bedside method to monitor ICP and cerebral vasospasm. It measures the velocity of RBC's flowing through the major vessels at the base of brain. Velocity increases through systole and decreases in diastole. Blood in the center of the vessel lumen travels faster than near the vessel wall, producing a spectrum of flow velocities. The spectrum produces the shape of a waveform obtained from arterial pressure trace. TCD measurements are usually obtained from the middle cerebral artery (MCA) territory. Marked reductions in MCA flow velocity signifies reduced cerebral perfusion pressure (CPP) in the setting of raised ICP. As ICP increases, the following sequence of changes occurs in TCD. First loss of diastolic flow, progressing to isolated systolic spike of flow and then to oscillating flow pattern, which signifies the onset of brain death. An absent signal should however be verified from other vessels as MCA signal may not be detected in older individuals when the temporal bones are ossified. Pulsatility index derived from TCD waveform correlates with CPP. TCD can be used in place of invasive ICP monitors with a fair degree of accuracy. When used in conjunction with vasodilating challenges (e.g. inhaled CO_2), TCD measurements may assist the clinician in assessing cerebrovascular reserve.

Jugular bulb oxygen saturation (SvO_2): Catheter is advanced in a retrograde manner, preferably under fluoroscopic guidance, into the right internal jugular vein (IJV) until its tip lies in the jugular bulb. Saturation of blood measured from this area provides a reflection of the cerebral oxygen demand/supply ratio. Fiberoptic devices that provide continuous measurements are also available. Falling SvO_2 is a sign of cerebral ischemia and can help in guiding therapy. Problems with this technique are many, the most important of which is the false negative result. Blood in the jugular venous bulb is derived from both sides of brain. Thus SvO_2 measures global balance between cerebral oxygen supply and demand. Inadequate CBF from a localized area may be masked by blood with higher SvO_2 from adequately perfused areas of the brain. Placement of even unilateral jugular venous catheters itself can impede cerebral venous return to raise ICP in patients with decreased intracranial compliance. Many neurointensivists strongly believe that SvO_2 monitoring is an important tool in managing patients with trauma and intracerebral hemorrhage.

Near infrared spectroscopy (NIRS): Offers the opportunity to assess the adequacy of brain oxygenation continuously and non-invasively. Near-infrared light penetrates the skull and during transmission through or reflection from brain tissue, undergoes changes in wavelength that are proportional to relative concentrations of oxygenated and deoxygenated hemoglobin in tissue beneath the field. Extensive preclinical and clinical data demonstrates that NIRS detects qualitative changes in brain oxygenation. NIRS may be useful for monitoring trends than for actual quantification of brain tissue oxygenation.

Regional Oxygenation probes and microdialysis techniques: This may be the ultimate future in cerebral oximetry. Zauner et al have reported their experience with a probe that measures intraparenchymal pO_2, pCO_2 and pH[5]. The probe uses fiberoptics and is introduced via a subarachnoid bolt. A microdialysis probe was also used to monitor

glucose and lactate. In 24 severely head injured patients, rpO_2 values < 20 mm Hg correlated with poor outcome. In individual patients, trends in gas tensions and glucose and lactate appeared to reflect improving or deteriorating metabolic status.

Multimodality monitoring: While individual monitors, though valuable have their own shortcomings, use of multiple monitors allows correlation and cross validation of data. This will help in guiding therapy better.

I. GENERAL MEASURES

A. Brain oriented life support [6,7,8] : **Basic physiological premises suggest the benefit of maintaining cerebral blood flow and oxygenation, and these assumptions are confirmed by data from the Traumatic Coma Data Bank (TCDB) and from other sources which demonstrate the detrimental effects of hypotension (systolic blood pressure < 90 mmHg) and hypoxia (PaO2 levels < 60 mm of Hg) in the early and later phases of head injury on outcome[9]. Hypotension and low cardiac output are deleterious to an already compromised brain. CVP should be maintained at 8 – 10 cm of water. Hypotension should be treated fast by administering IV fluids, blood or ionotropes as appropriate in a given situation. Hypoxia and hypercapnia cause further cerebral injury and need to be strictly avoided. Mechanical ventilation and PEEP is generally required to optimize oxygenation. Normal acid base balance is desirable. Metabolic acidosis and respiratory alkalosis are the common disturbance that needs to be treated. Normovolemia should be maintained: hypervolemia increases brain edema while excessive dehydration decreases CBF. Normal serum osmolality and oncotic pressure need to be maintained. Hyponatremia needs to be corrected as it exaggerates brain edema and also precipitates seizures. Hyperglycemia is associated with worsening of neurological injury in head injury. Hyperthermia aggravates neurological injury. Normothermia should be achieved by measures such as cold sponging, cooling blankets and antipyretics. Systemic infections should be appropriately treated.** [6,7]**.**

B. Fluid therapy: Fluid replacement should be guided by clinical and laboratory assessment of volume status and by invasive hemodynamic monitoring, but generally involves the administration of 30–40 ml/kg of maintenance fluid per day. The choice of hydration fluid is largely based on inconclusive results from animal data. Unlike other vascular beds, capillaries in the brain are impermeable to most small molecules, and fluid flux across the normal BBB is governed by osmolarity rather than oncotic pressure. Consequently, hypotonic fluids are avoided and serum osmolality is maintained at high normal/levels (290–300 mosm/l in our practice) to minimize fluid flux into the injured brain. Dextrose containing solutions are avoided since the residual free water after dextrose metabolism can worsen cerebral edema, and the associated elevations in blood sugar may worsen outcome. Quershi et al used 3% saline in patients with brain edema due to head injury and demonstrated a rise in plasma sodium and osmolality and at least temporary reduction in ICP and midline shift [10.] Simma et al reported that hypertonic saline (sodium 268mmol/L, 598mOsm/L) when compared to lactated Ringer's solution as maintenance fluid in head injured children, resulted in lower ICP values, less need for barbiturate therapy, a lower incidence of acute lung injury, fewer complications and a shorter ICU stay[11]. Maintenance of oncotic pressure with albumin supplements is one of the cornerstones of the Lund protocol, and other authors have discussed the advantages of colloid use in this setting [12]. Both albumin and gelatins have been used, but hetastarch should be used with caution, since its effects on hemostasis may potentiate intracranial hemorrhage. There is some evidence indicating that certain colloids (pentastarch) may be effective in reducing the cerebral edema associated with cerebral ischemic and reperfusion injury. Agents which 'plug leaks' by acting as oxygen free radical scavengers and or by inhibiting neutrophil adhesion may be the resuscitation fluids of the future. [6,7]

C. **Nutrition**: Head injured patients have high nutritional requirements and feeding should be instituted early (within 24 h), aiming to replace 140% of resting metabolic expenditure (with 15% of calories supplied as protein) by the seventh day post trauma. Enteral feeding is preferred, as it tends to be associated with a lower incidence of hyperglycemia and because of its protective effect against gastric ulceration, the incidence of which may be increased in these patients. Impaired gastric emptying is a common finding in head injury, and can be treated with prokinetic agents, such as cisapride and metoclopramide. In those who cannot be fed enterally, parenteral nutrition should be considered together with some form of prophylaxis against gastric ulceration (H2 antagonists or sucralfate) and rigorous blood sugar control.

D. **Antiepileptic therapy:** Seizures occurs both early (< 7 days) or late (> 7 days) after head injury, with a reported incidence of between 4–25% and 9–42%, respectively. Seizure prophylaxis with phenytoin or carbamazepine can reduce the incidence of early post-traumatic epilepsy, but has little impact on late seizures, neurological outcome

or mortality. The incidence of posttraumatic seizures is greatest in patients with a GCS < 10, and in the presence of an intracranial hematoma, contusion, penetrating injury or depressed skull fractures. Since it is important to balance the possible benefit from seizure reduction against the side effects of anti epileptic drugs, such patients may form the most appropriate subgroup for acute (days to weeks) seizure prophylaxis following head injury. [6,7]

II. CEREBRAL BLOOD FLOW PROMOTION TECHNIQUES [8]

The ultimate object is to provide brain cells with the amount of O_2 and glucose that covers their energy requirements for both functional needs and to circumvent the crisis. Against energy failure we have two lines of protection: hemodynamic and metabolic. Hemodynamic protection composes attempts at restoring circulation or at improving its efficiency via manipulation of blood pressure, vasoreactivity and blood rheology. [8] The alternative strategy is to reduce the needs by lowering CMRO2.

Available oxygen = CBF X Hemoglobin X Saturation.

Available oxygen can thus be improved by a) Increasing CBF essentially by improving CPP b) Improving hemoglobin if the patient has clinically significant anemia. c) Improving SO2: Intentional hyperoxia has been documented to reverse the cerebral oxygen desaturation and anaerobic metabolism in head injured patients.

Cerebral Perfusion Pressure (CPP) = MAP - ICP

A) **MAP Targeted treatment**: When cerebral autoregulation is intact the cerebral blood flow is kept constant despite changes in CPP between 60 mm and 140 mm. The controversy centers on the minimum level of CPP that is adequate in brain injury. Most centers would agree on the need to maintain cerebral perfusion by keeping CPP well above 60–70 mmHg, either by decreasing ICP or by increasing MAP. Despite this large body of data that supports the maintenance of high CPP values in head injury, there is some concern that relatively high perfusion pressures may contribute to edema formation after head injury. A recent study comparing CBF targeted management (CPP> 70, PCO2= 35) with ICP targeted therapy (ICP <25, PCO2 up to 25, CPP> 50) found no difference in the outcome. There are however, data that show that ICP is an independent, albeit weaker, determinant of outcome in severe head injury and a recent study in fact concluded that CPP has correlation with outcome only when CPP was below 60 mm Hg. Above 60 mm CPP had no correlation with outcome suggesting that higher CPP does not always translate itself into better outcome. The different schools of thought on CPP targeted therapy can be summarized as follows[12]

Rosner et al's Approach – Optimizing cerebral perfusion by CPP management.: This approach is based on the concept that normal autoregulatory response to reduced CPP causes dilatation of the cerebral blood vessels .This results in an increase in ICP causing further reduction in CPP, thus setting up a cycle that leads to ever reducing CPP. Under these circumstances an increase in arterial blood pressure would break the cycle and reduce ICP. This approach is widely practiced and recommended.

Lund Therapy approach: This approach centers on reduction in microvascular pressures to minimize edema formation in the brain. Colloid osmotic pressure is maintained near normal values using infusion of albumin and erythrocytes. Capillary hydrostatic pressure is decreased by reducing systemic blood pressure using betablockers and clonidine. In addition low dose thiopental and dihydroergotamine are used to reduce cerebral blood volume by constricting precapillary resistance vessels.

Miller et al's Balanced approach: This approach attempts to direct the treatment to the underlying pathophysiology. Miller et al proposed sedative agents for intracranial hypertension of vascular origin, and osmotic agents for intracranial hypertension due to interstitial edema.

Zero flow pressure: Remodeling of cerebral circulation: The concept of zero flow pressure (ZFP) and the critical closing pressure has been introduced recently and is still being debated. Vascular tone, compliance and other physical properties may play an important role in determining the effective downstream pressure in cerebral circulation. Estimation of ZFP allows estimation of changes in the downstream pressure non-invasively, usually by TCD. All these methods use extrapolation of instantaneous values of middle cerebral artery flow velocity and blood pressure at which blood flow would cease, defining the ZFP. Therefore, in subjects without raised ICP,

CPP= MAP- ZFP.

More work is required to ascertain its importance in trauma, but there may be exciting opportunities to manipulate the downstream pressure to increase CPP without having to increase the MAP. [8,9]

B) Decreasing ICP: This involves

i) Decompression:

ii) Hyperventilation

iii) Hypersomolar therapy

iv) CNS depressants (typically barbiturates)

Decompression: Drainage of CSF and surgical decompression (whenever possible): Data quoted in the Brain Trauma Foundation guidelines for the management of severe head injury provide circumstantial evidence supporting the increased use of CSF drainage for ICP control though it did not improve outcome[13].

Hyperventilation: Controlled hyperventilation is a time-tested means of reducing ICP by means of reducing the CBF and CBV over the short term. Its routine use in all situations is now subject of much debate. CBF and CBV have a linear relationship with $PaCO_2$. If $PaCO_2$ is reduced below 20 mm Hg, cerebral ischemia can result. For hyperventilation to be a useful clinical tool, $PaCO_2$ should be kept between 20-30 mm Hg. Hyperventilation might exert a protective effect on focal cerebral ischemia by vasoconstricting the normal cerebral vasculature, thereby shunting the normal blood to the ischemic area (Robin Hood effect). In addition to concerns regarding ischemia, hyperventilation may have only short-lived effectiveness in decreasing ICP. The drawback with hyperventilation is that on prolonged use, compensatory reductions in cerebral extracellular fluid (ECF) bicarbonate levels rapidly restore ECF pH and over time, attenuate the effect of low $PaCO_2$ levels on vascular tone. These cerebral vasocnstrictive effects of hypocapnia should be applied with the knowledge that in healthy volunteers CO2 was associated with an increase in zero flow pressure and decrease in CPP [14].

Hyperosmolar therapy:

In the setting of clinical, radiological or measured evidence of intracranial hypertension, mannitol (0.25–1 g/kg, usually as a 20% solution) has traditionally been used to elevate plasma osmolarity and reduce brain edema. In addition to its osmotic effects, mannitol probably reduces ICP by improving CPP and microcirculatory dynamics. Some of mannitol's potentially beneficial effects include increased blood viscosity & free radicals scavenging and antioxidant activity. Side effects include secondary increases in ICP when the BBB is disrupted, fluid overload from initial intra vascular volume expansion, and renal toxicity from excessive use. These can be minimized if its use is discontinued when it no longer produces significant ICP reduction, volume status is monitored and if plasma osmolality is not allowed to rise above 320 mosm/l (although there is little objective evidence to support this threshold). In addition to their use as maintenance fluids, hypertonic saline solutions (7.5%) are being used for small volume resuscitations, and may provide improve outcome in comatose patients suffering from multiple trauma. Recent reports also highlight the successful use of 23.4% saline for treatment of intracranial hypertension refractory to mannitol [15]. While more studies are required, it appears hypertonic saline will find a place in the treatment of brain swelling

Sedation and neuromuscular blockade: Intravenous sedating agents preserve autoregulation and the cerebrovascular response to CO2, even at doses sufficient to abolish cortical activity, and decrease cerebral blood flow, cerebral metabolism and ICP. The reduction in flow is secondary to a reduction in metabolism (flow-metabolism coupling). Barbiturates are now less commonly used in the head injured patient for routine sedation, owing to the availability of other agents, such as propofol, which possess similar cerebrovascular effects but better pharmacokinetic profiles. However, propofol is not without side effects. At high doses, propofol can induce hypotension and decrease in cerebral perfusion pressure. Midazolam is often used in combination with fentanyl and propofol for sedating the patient with head injury. Midazolam reduces $CMRO_2$, CBF and CBV with both cerebral autoregulation and vasoreactivity to CO_2 remaining intact. However, these effects are inconsistent and transient, and even large doses of midazolam will not produce burst suppression or an isoelectric EEG [1]. Opioids generally have negligible effects on CBF and CMRO2. However, the newer synthetic opioids fentanyl, sufentanil and alfentanil, can increase ICP in patients with tumors and head trauma. This increase, originally assumed to be secondary to an increase in CBF, is more likely to be the result of changes in PaCO2 and systemic hypotension and can be avoided if blood pressure and ventilation are controlled.

Neuromuscular blockade in the head injured patient receiving intensive care is currently the subject of much debate. The use of neuromuscular blockers can play an important role in the head injured patient. Coughing and 'bucking on the tube' can result in an increase in ICP, and the administration of non-depolarizing muscle relaxants prevents such rises in ICP. However, despite facilitation of ICP control, use of these agents is not associated with better outcomes, perhaps because of increased respiratory complications. Further, long term use of neuromuscular blockade has been associated with continued paralysis after drug discontinuation and acute myopathy. However, atracurium is non-cumulative and has not been associated with myopathy, and theoretical concerns about the accumulation of laudanosine, a cerebral excitatory metabolite of atracurium, in head injured patients have not been shown to be clinically relevant [1].

III. REDUCING CEREBRAL METABOLISM

A. Hypothermia: Hypothermia progressively depresses the cerebral metabolism, both the activation metabolism as well as the residual metabolism. Metabolism decreases linearly from 6 to 10% for each one-degree decrease in temperature in the range 35 to 25 degrees. The protective mechanism may not entirely be due to decrease in metabolism but also due to its membrane stabilization, preservation of ion homeostasis, decrease in excitatory neurotransmitter release, decrease in calcium influx, prevention of lipid peroxidation, and sustained suppression of cytokines, particularly interleukin [1]. Deep hypothermic circulatory arrest, which is employed during complex congenital cardiac surgeries and surgery on the aortic arch, involves cooling the patient on cardiopulmonary bypass to a temperature of 18°C. At this temperature the brain is protected from ischemia for a period of 45-60 minutes.

Use of hypothermia carries with it many disadvantages. It causes an increase in the afterload to the heart by increasing the peripheral vascular resistance and by increasing the blood viscosity. Hypothermia also causes diuresis by suppressing the anti diuretic hormone and predisposes the patient to hypovolemia. Hypothermia also has the potential to cause more myocardial ischemia. This may in part be due to the post-anesthetic shivering which increases the myocardial oxygen demand. Hypothermia also reduces the ventricular contractility and diastolic relaxation and reduces the response of the heart to ionotropic medications. Ventricular fibrillation can occur below 30°C that may prove refractory to treatment. Rewarming phase from hypothermia may be complicated by reduced oxygenation, pulmonary edema and raised ICP. Hypothermia can cause coagulation abnormalities and predispose the patient to infection by depression of immunologic status.

One of the early studies on hypothermia, the NABIS study by Clifton et al in 1994 was halted after 392 patients, as the treatment was not effective [18]. Some important points from the study are that older patients not only do not benefit from the hypothermia, they also do worse than normothermics. Also if patients are hypothermic on admission it is not advisable to warm them to normothermia. The timing of initiation might also be important with early induction of hypothermia giving better results. Similarly it was shown that hypothermia did have a beneficial effect on the proportion of patients with high intracranial pressure. Thus, it is important however not to entirely dismiss the role of hypothermia in achieving cerebral protection and may still be used in patients with cardiac arrest, pediatric head injury etc [19,20].

The Cochrane review analyzing 12 trials with 812 patients could not find a statistical reduction in mortality in patients receiving mild hypothermia either early or deferred. There is no evidence that hypothermia is beneficial in the treatment of head injury. The earlier, encouraging, trial results have not been repeated in larger trials. The reasons for this are unclear. Hypothermia increases the risk of pneumonia and has other potentially harmful side effects [21]. The Intraoperative hypothermia for aneurysm surgery trial (IHAST), a randomized multicentric trial in "good grade" patients (WFNS I, II and III) who had subarachnoid hemorrhage of less than 14 days, found no benefit with mild intra-operative hypothermia of up to 33^{o}C [22]. The results of the Hypothermia in Pediatric Head Injury Trial (Hyp-HIT), which finished, at the end 2004 should be available soon and should shed more light on its effect in pediatric patient population.

B) Barbiturates: Their primary effect is via the reduction in $CMRO_2$, thereby increasing ratio of oxygen supply to demand. Their greatest effect is seen in reduction of energy requirement for neuronal function. But once isoelectric EEG is established, the cerebral oxygen consumption reduction that can be achieved by barbiturates is exhausted. The reduction in $CMRO_2$ is accompanied by reduction in CBF and ICP. They also help in reducing cerebral edema and decrease CSF secretion. Barbiturates may also shunt blood between normal and ischemic areas of the brain. It also suppresses seizures, reduces catecholamine-induced hyperactivity, scavenges free radicals and stabilizes membranes.

Their role in focal and cerebral ischemia merit further attention. Recall that global ischemia produces EEG suppression in 15-30 seconds when almost all-electrical activity is abolished and basal metabolism is reduced. In such a scenario, barbiturates can confer no further protection. Because of this there is no role for barbiturates in cerebral resuscitation following cardiac arrest where the brain has experienced global ischemia. In focal ischemia, where there is continuing neuronal activity, barbiturates slows down metabolism and can help in improving the tolerance to ischemia. An 'inverse steal' phenomenon is also described whereby the blood flow from the normal areas gets shunted to the ischemic area by the vasoconstriction produced by barbiturates. In focal ischemia, the success achieved in animal trials could not be duplicated in humans. The reasons for this could be multifactorial and may include associated comorbidity,

associated extensive cerebral vascular pathology, cardiovascular and respiratory effects of barbiturates, type, dose, timing and duration of barbiturate administration etc[7]. There is little reliable clinical evidence other than anecdotal reports that attest to the efficacy of barbiturates in preventing or treating focal ischemia.

Despite poor clinical evidence enthusiasm for this mode of therapy continues on the basis of a few encouraging case studies. Levine et al compared two groups of patients undergoing MCA aneurysm clipping. Before temporary clipping, the study group was given barbiturate and the control group was not given barbiturate. The incidence of cerebral ischemia was found to be 45% in the control group and 15% in the barbiturate group [23]. There are similar reports of beneficial effects in specific patient populations such as during cardiopulmonary bypass procedures requiring an open ventricle, extracranial to intracranial procedures, deliberate profound hypotension and carotid endarterectomy [1]. The use of barbiturates in the above surgeries is by no means mandatory and individual intensive care/ anesthesia units should have their own protocol for when and how to start barbiturate coma.

The appropriate dose of barbiturate for barbiturate coma is one that causes EEG suppression. Thiopentone in a dose of 3-7mg/Kg will produce EEG burst suppression for about 5-10 minutes. If temporary clipping is planned during aneurysm surgery, the above dose may suffice. High dose regime recommended in situations of focal ischemia to produce burst suppression on EEG [31] consists of loading dose of 25 to 50 mgkg-1. This is followed by an infusion 2 to 10 mgkg-1hr^{-1} .The low dose regime of 3mg/ Kg of Thiopentone followed by 1-2 mg/Kg/ hr is enough to produce reductions in ICP. If the goal is burst suppression on EEG, the same must be verified by monitoring the EEG. Post-operative patients on barbiturate infusions should continue to receive regular analgesic medications (preferably opioids) especially before intensive care procedures such as endotracheal suctioning.

Timing of barbiturate therapy [23]**:** Cerebral protection is best initiated prior to the occurrence of brain ischemia. Barbiturate therapy appears to provide some benefit even if administered after a focal ischemic insult. Barbiturates have been shown to diminish infarct size (animal study) when administered after focal ischaemia.

Duration of barbiturate therapy: When used prophylactically, therapy is usually discontinued when the period of potential or actual insult is over [23] The duration of therapy when instituted after an insult is controversial and has varied from bolus doses to infusions for 24 to 72 hours or more. The long duration has been advocated because post insult injury may last for this period & cerebral edema peaks at 48 hours after an ischemic injury[23]

There are dangers associated with barbiturate coma. Most important of which is sever depression of cardiac function that should be supported with augmentation of blood volume and/or the use of vasoactive agents. The cardiac depression itself has the potential to decrease the CPP. Barbiturates also cause loss of thermoregulation and make patients susceptible to infections. Time taken to awaken from barbiturate coma can by itself extend to more than 48 hours and thereby not only is the assessment of neurological status delayed, the patients will require prolonged mechanical ventilatory support as well.

The best source of review for this subject is the guidelines for the management of severe traumatic brain injury patients – a joint venture of the BTF, AANS and the joint section of the neurotrauma and critical care. The guidelines say that "high dose barbiturate therapy can be considered in hemodynamicaly stable salvageable severe head injury with increased ICP, refractory to conventional medical /surgical management". Two lab studies and one clinical study have clarified the role of barbiturate in ischemia once and for all – barbiturate narcosis is of no benefit in global ischemia and may be of variable use in some cases of focal ischemia and in reducing neuropsychiatric complications in CPB. [24,25]

C) Propofol: The metabolic changes resulting from propofol anesthesia closely resemble the homogenous depression of CMR caused by barbiturates. Propofol decreases EEG activity with concurrent reductions in CMRO2 and CBF with an increase in cerebrovascular resistance. Propofol also reduces voltage-activated sodium channel conductance at concentrations within the clinical range. Its antioxidant properties may also be of benefit. It may also attenuate neurotransmitter release during ischemia. Propofol has been reported to provide some brain protection in hypoxia and incomplete global ischemia. Prompt awakening following cessation is an added attraction of using propofol. High doses may produce hypotension, which reverses rapidly upon discontinuation (usually within 5-10 minutes). Administration of propofol to head injured patients with elevated ICP has been associated with a reduction in ICP but also of CPP. Propofol infusion titrated to produce unresponsiveness (8 mgkg-1hr-1) in humans, resulted in 55% depression in CMR for glucose, as measured using positron emission tomography [26] There are reports of propofol-induced seizure like activity, myoclonus and opisthotonus, which are clearly undesirable in neurologically injured patients. Besides the use of propofol for more than 48 hours can be complicated by propofol infusion syndrome, which has the potential to be fatal. Clearly, the use of propofol in cerebral protection cannot be advocated until the results of more clinical studies become available.

IV. PHARMACOLOGICAL NEUROPROTECTION

Anesthetic agents are generally considered to be neuroprotective as they depress the cerebral metabolic rate. There are many other pharmacological effects, which may contribute to neuroprotection, these are, reduction of ICP, anti-convulsant action, free radical scavenging, drug-induced inverse steal, antagonism at voltage-sensitive calcium or sodium channels or ligand gated calcium channels, potentiation of GABAergic transmission or attenuation of ischemia induced neurotransmitter release.

a) Isoflurane: Volatile anesthetics are also capable of decreasing neuronal activity on the EEG with an accompanying decrease in CMRO2 and CBF. The hemodynamic profile and recovery characteristics of isoflurane are far superior to barbiturates. Isoflurane (as well as sevoflurane and desflurane) are capable of inducing a level of anesthesia that suppresses the EEG activity (to the point of isoelectricity) without significantly affecting the hemodynamics. In models of incomplete ischemia, isoflurane has been shown to be protective but not in global ischemia. Mechanism of action of isoflurane includes metabolic suppression, prevention of a cerebral hyperthermic response to ischemia, suppression of sympathetic activity, and a decrease in glutamate receptors preventing Ca influx and Ca cascade. The EEG signs of cerebral ischemia were late to occur in patients undergoing carotid endarterectomy when they are on isoflurane than during anesthesia with halothane or neuroleptanesthesia.

b) Ketamine: It is a non-competitive antagonist of glutamate receptors (NMDA-subtype). There is little current evidence to support its use.

c) Nitrous oxide: N_2O may affect cerebral protection provided by other agents. N_2O almost always produces an increase in CBF and $CMRO_2$ in humans. This is due to stimulation of sympathetic activity by N_2O. It is also suggested that the use of N_2O may worsen neurologic outcome and the concurrent use of other anesthetic agents may attenuate this effect [1].

d) Etomidate: It is a cardio-stable induction agent that produces dose-dependent reduction in CBF and $CMRO_2$. It is also a direct cerebral vasoconstrictor, which reduces the CBF independent of its effect on cerebral metabolism. Under etomidate anesthesia, the CO_2 reactivity remains intact. Etomidate scores over barbiturate in that it does not produce profound hypotension. But the enthusiasm for etomidate has been dampened by two complications, adrenocortical suppression induced by long-term etomidate and myoclonic activity [1].

e) Local anesthetics: Lignocaine blocks Na^+ channels the cell that restricts Na^+ influx and K^+ efflux. The work done by the membrane bound ion-pumps is thus reduced and hence may also reduce the energy requirements of ion homeostasis. In ischemic brain Lidocaine also reduces the $CMRO_2$. High dose Lidocaine has direct toxic effect on oxidative phosphorylation and can depress circulation. Based on current evidence, there is little role for lignocaine in this setting [1].

f) Magnesium: It acts on ischemic brain by antagonizing the effects of Ca, inhibiting glutamate release and producing NMDA receptor blockade. Magnesium works well in ischemic animal models. It reduces infarct volume and improved neurological outcome in a rat model of focal ischemia. The IMAGES trial (Intravenous Magnesium Efficacy in Stroke), a randomized multicenter, double blind, placebo-controlled trial was done in patients who presented within 12 hours of acute ischemic stroke, who had been experiencing limb weakness for at least 1 hour, and who were previously independent. The results were disappointing with no change in the intervention group in terms of death or disability at 90 days compared to the control group [27].

g) Calcium channel blockers: With the knowledge that damage is inflicted on the cell due to its inability to clear intracytoplasmic calcium, it is intuitive to use calcium antagonists in cerebral ischemia as these drugs block the influx of Ca^+ thought the voltage sensitive ion channels. The source of Ca necessary for large cerebral arteries is extracellular, unlike systemic arteries, which use bound intracellular pool of Ca. This makes cerebral vessels exquisitely sensitive to calcium channel blockers.

Lidoflazine was the one of the first drug of this class to undergo trial and fail. Nimodipine was the next drug that failed to show any benefit in survivors of cardiac arrest. Improved outcome was noted in survivors of > 10 minutes of cardiac arrest [28]. Two major head injury trials (HIT I and HIT II) showed no statistically significant improvement in outcome at the end of six months [29, 30]. However, HIT II showed a 10% improvement in the subgroup of patients who had sustained traumatic subarachnoid hemorrhage (t-SAH). Harders et al have also confirmed the beneficial effect of Nimodipine in t-SAH [31]. The Cochrane data base review was inconclusive about the ability of calcium channel blockers in head injury to reduce disability and death [32].

The role of nimodipine in preventing cerebral vasospasm has been extensively studied. Studies show that nimodipine can reduce the incidence of delayed ischemic deficits following SAH and improves the neurologic outcome. Nimodipine produces the most improvement in patients with moderate symptoms but produces no change in patients with severe symptoms. Nimodipine has no effect on the extent and severity of vasospasm as demonstrated by angiography. The administration of oral nimodipine 60 mg four times a day is practiced in patients who have SAH due to aneurysm rupture [33].

In focal ischemia nimodipine has been shown in early trials to decrease infarct size and improve neurologic recovery. It increases the regional CBF to the ischemic hemisphere by an inverse steal mechanism ('Robin Hood') effect. The recovery was greatest in those with mild to moderate deficits, when the drug was initiated within 12 hours of insult. This suggests that nimodipine exerts its beneficial effect by its action on ischemic penumbra. If the ischemia is mild, nimodipine may improve CBF to restore neurological function [34]. The early success with nimodipine could not be duplicated by subsequent trials and one intravenous nimodipine trial suggests that its use may actually be detrimental [35].

h) Steroids: Corticosteroids stabilize the membranes, reduce cerebral edema, scavenge free radicals, reduce CSF production and increase the seizure threshold. The anti-cerebral edema effects of steroids are best seen in peri-tumoral edema. High and low dose steroid produced no improvement in patients with traumatic brain injury. Grumme et al have shown that triamcinolone improves neurologic recovery and decreases mortality [36]. Alderson et al in a meta-analysis suggested a 1.8% pooled risk reduction for death in patients who received steroids [37]. Cochrane review concluded that neither moderate benefit nor adverse effect of steroid could be confirmed [38]. A large multi-center trial, the Corticosteroid randomization after significant head injury trial (CRASH) has concluded that "corticosteroids should not be routinely used in head injury" [39].

i) Glutamate Antagonists and other Neurotransmitter Modulators [2]: Glutamate alone activates three different ion channels, NMDA, AMPA and kainite. Excessive stimulation of NMDA receptors is neurotoxic. NMDA receptor antagonists are either competitive i.e. they compete with excitatory amino acids for receptor binding or noncompetitive i.e. bind directly to the receptor itself and prevent calcium influx. Ketamine is a non-competitive NMDA antagonist. The promise of this group of drugs remains confined to preclinical and animal studies. In those settings, NMDA antagonists have shown to be protective of the penumbral neurons. Atleast three clinical studies of three different NMDA antagonists were cancelled during phase III trials due to drug toxicity. Further research in this direction is still continuing and focuses on presynaptic inhibitors of glutamate release, AMPA receptor antagonists, dopamine D1 antagonists and GAB agonists [2].

j) Lubeluzole [2]: A novel benzathiazole derivative has been shown to be neuroprotective in animal models of focal cerebral ischemia. This drug inhibits glutamate release and reduces potassium-related increases in intracellular Ca. Clinical trials are yet to show convincing evidence of beneficial effect in humans.

k) Free radicals [2]: Normal free radical scavengers include vitamin C and E, catalase and superoxide dismutase. Mitochondrial failure leads to release of free radicals and the native scavenger systems become saturated, allowing free radicals to damage cell contents. The drug tirilazad mesylate is a potent free radical scavenger, which has shown promising results in preclinical trials. Clinical trials in ischemic stroke showed no advantage with the use of this drug. However there is some evidence that it improves mortality in poor grade SAH patients (grade IV and V)

l) Nitric Oxide [2]: NO is water and lipid soluble free radical with diverse biologic properties. Under normal conditions NO is produced in small, regulated concentrations from L-arginine by nitric oxide synthase (NOS). In ischemic brain there is an acute increase NO. The release of NO has several positive and negative effects during cerebral ischemia, depending on the timing or the source of production. Three possible sources of NO production can be identified.

a) nNO from neuronal NOS (nNOS). This is an acute increase and returns to normal by about 60 minutes

b) eNO from endothelial NOS (eNOS). This lasts for several hours but is followed by prolonged increases over the periphery of the infarction.

c) iNO from inducible NOS (iNOS). This is from infiltrating neutrophils, astrocytes etc. This starts appearing by 6-12 hours and remains elevated for many days.

Increased release of eNO is neuroprotective, probably by increasing CBF through its effects on vascular smooth muscle but also by inhibiting platelet aggregation and leukocyte adhesion Enhancing eNOS-mediated release of NO with NO donor sodium nitroprusside resulted in smaller cerebral infarcts in animals. In contrast, nNO increases ischemic injury due to free radical release. NO combines with superoxide to form peroxynitrite, which is more toxic than either of its precursors. In laboratory, inhibition of nNOS with 7-nitroindazole, significantly reduces infarct volume in focal ischemia. An attractive hypothetical treatment regime would involve selective augmentation of eNOS by NO donors and suppression of nNOS by selective inhibitors. The drawback is that the neuroprotective effect of these drugs is lost after 2 hours and the effects of global inhibition such as nNOS, which is important for neuronal transmission, may have unknown risks. The inhibition of iNOS offers another possible target. Aminoguanidine, an inhibitor of iNOS, reduces infarct volume in rat stroke model. Treatment was found to be effective even when started 24 hours after infarct.

m) Leukocyte adhesion: Rapid inflammatory response, which is coupled with the release of inflammatory mediators, inflicts most of the secondary injury following ischemia. The adhesion of the leukocyte to the endothelium involves interaction with atleast three types of adhesion molecules. These adhesion molecules have been targeted as a means of cerebral protection. The studies showed promising results in animal models following transient focal ischemia. Clinical trials with a similar class of drug had unacceptable side effect profile.

Conclusion: Effective, fail-safe, pharmacologic neuroprotection still continues to elude us. Though the pathophysiology of cerebral ischemia is now known, this has not automatically translated into success with any new pharmacologic agent. There is disparity between animal studies (where most of the so called neuroprotective agents are effective) and human clinical trials. Many reasons for this have been cited [7]. Active research is continuing in this area and more breakthroughs are likely.

References

1. Milde LN. Cerebral Protection in Clinical Neuroanesthesia. Cucchiara RF, Black S and Michenfelder JD (ed) 2nd ed. Churchill Livingstone, NY: 1998, 177-228

2. Zabramski JM and Albuquerque FC. Cerebral Protection in Management of cerebral aneurysms. Le Roux PD, Winn HR and Newell DW (ed) Saunders, Pennsylvania, 2004, 547-562

3. Kass IS and Cottrell JE. Pathophysiology of brain injury in Anesthesia and Neurosurgery. Cottrell JE and Smith DS (ed) 4th ed. Mosby, Philadelphia: 2001, 69-82

4. Diego DJ, Yancy V and Prough DS. Brain function monitoring in Textbook of critical care. Grenvik A, Ayres SM, Holbrook PR and Shoemaker WS (ed). 4th ed. Sanders, Philadelphia: 2000, 1813-1824

5. Zauner A, Doppenberg EMR, Woodward JJ et al: Continuous monitoring of cerebral substrate delivery and clearance: Initial experience in 24 patients with sever acute brain injuries. Neurosurgery, 41: 1997, 1082-1093.

6. Maas AIR, Dearden M, G M Taesdale et al. EBIC guidelines for management of severe head injury in adults. Acta Neurochir (Wein); 139:286-294, 1997

7. Rao GSU. Cerebral Protection – beyond barbiturates. Proceedings of the 5th ISNAAC, 261- 272, 2004.

8. Menon G, Bhattacharya RN and Nair S. Cerebral Protection current concepts.2 (2): 2005, 67-80

9. Chestnut RM, Marshall SB, Piek J et al: Early and late systemic hypotension as a frequent and fundamental source of cerebral ischemia following severe brain injury in the Traumatic Coma Data Bank. Acta Neurochir Suppl (Wien). 1993; 59:121-5.

10. Qureshi AI, Suarez JI, Bhardwaj A, et al: Use of hypertonic (3%) saline/ acetate infusion in the treatment of cerebral edema: Effect on intracranial pressure and lateral displacement of the brain. Crit Care Med. 6(3): 1998, 440-6.

11. Simma B, Burger R, Falk M, et al: A prospective, randomized, and controlled study of fluid management in children with severe head injury: lactated Ringer's solution versus hypertonic saline. Crit Care Med. 1998 Jul; 26(7): 1265-70.

12. Mahajan RP. Zero flow pressure: Remodelling cerebral circulation? . Proceedings of the 5th ISNAAC, 249-254, 2004.

13. Munch E, Horn P, Schurer L et al: Management of severe traumatic brain injury by decompressive craniectomy. Neurosurgery. 47(2): 2000 315-22.

14. Hancock SM, Mahajan RP, and Athanassiou L: Non-invasive estimation of cerebral perfusion pressure and zero flow pressure in healthy volunteers. Effects of changes in end-tidal carbon dioxide. Anesth Analg 96: 2003, 847-51

15. Ware ML, Nemani VM, Meeker M, Lee C et al. Effects of 23.4% sodium chloride solution in reducing intracranial pressure in patients with traumatic brain injury: a preliminary study. Neurosurgery. 57(4): 2005:727-36

16. Hsiang JK, Chesnut RM, Crisp CB et al: Early, routine paralysis for intracranial pressure control in severe head injury: is it necessary? Crit Care Med. 22(9): 1994, 1471-6.

17. Sreedhar R, Gandhinglkar SV. Pharmacological Neuroprotection. Indian J Anesthesia. 47(1), 2003: 8 –22.

18. Clifton GL, Miller ER, Choi SC et al: Lack of effect of hypothermia in acute brain injury. The National Acute Brain Injury Study: (NABIS: H): A Multicenter Trial. New England Journal of Medicine 344(8): 2202, 556-563.

19. Clifton GL. Is keeping cool still hot? An update on hypothermia in brain injury. Curr Opin Crit care. 10(2), 2004: 116 –9

20. Setlur R. Mild hypothermia for head injury – does it work? Proceedings of the 5th ISNAAC, 311- 316, 2004.

21. Aldrson P, Gadkary C and Signorini DF. Therapeutic hypothermia for head injury. The Cochrane data of systemic reviews. 2006 Issue1.http:// www.cochrane.org/reviews/en/ab/001048.html. Accessed on 14/2/2006

22. Mild Intraoperative Hypothermia during Surgery for Intracranial Aneurysm. Todd M. M., Hindman B. J., Clarke W. R., Torner J. C., the Intraoperative **Hypothermia** for Aneurysm Surgery Trial (IHAST) Investigators N Engl J Med 2005; 352:135-145, Jan 13, 2005.

23. Levine SD, Masri LS, Levy ML et al: Temporary occlusion of middle cerebral artery in intracranial aneurysm surgery: time limitation and advantage of brain protection. J Neurosurg 87: 817-824, 1997

24. Cohadon F. Brain Protection. Advances and technical standards Vol 17 78-126,1995

25. Menon DK. Cerebral protection in severe brain injury: physiological determinants of outcome and their optimization. British Medical Bulletin 55 (no.1): 226 –258.

26. Kelly DF, Godale DB, Williams J al. Propofol in the treatment of moderate and severe head injury: a randomized, prospective double blinded pilot trial. J Neurosurg; 90: 1042- 1052,1999.

27. Muir KW, Lees KR, Ford I et al. Magnesium for acute stroke (Intravenous Magnesium Efficacy in Stroke trial): randomized controlled trial. for acute stroke. Lancet 363: 2004, 439-45

28. Brain resuscitation Clinical Study Group: A randomized clinical study of a calcium entry blocker (Lidoflazine) in the treatment of comatose survivors of cardiac arrest. N Engl J Med 324: 1225-1231

29. Bailey I, Bell A, Gray J et al. A trial of the effect of nimodipine on outcome after head injury. Acta Neurochir (Wien) 110: 1991, 97-105

30. European Study Group on nimodipine in severe head injury: A multicenter trial of the efficacy of nimodipine on outcome of severe head injury. J Neurosurg 80: 1994, 797-804

31. Harders A, Kakareika A, Braakman R and the German SAH study group. Traumatic subarachnoid hemorrhage and its treatment with nimodipine. J Neurosurg 85: 1996, 82-89

32. Langham J Goldfrad C, Teasdale G et al: Calcium channel blockers for acute traumatic brain injury. Cochrane Data Base Syst Rev 2: 2000, CD000565

33. Haley EC, Kassel NF, Tomer JC. A randomized controlled trial of high ode intravenous nicardipine in aneurismal subarachnoid hemorrhage: A report of co-operative aneurysm study. J Neurosurg. 78: 1993, 537-547
34. Gelmers HG, Gorter CJ, de Weerdt and Weizer HJA: A controlled trial of nimodipine in acute ischemic stroke. New Engl J Med. 318: 1988, 203
35. Wahlgren NG, McMahon DG, De Keyser J et al. The INWEST study group. Intravenous Nimodipine West European Stroke Trial (INWEST) of nimodipine in the treatment of acute ischemic stroke. Cerebrovasc Dis. 4A: 1994, 204
36. Grumme T, Baethmann A, Kolodziejczyk D et al. Treatment of patients with severe head injury by triamcinolone: a prospective controlled multicenter clinical trial of 396 cases. Res Exp Med (Berl), 195A: 1995, 217
37. Alderson P, Roberts I: Corticosteroids in acute traumatic brain injury: Systematic review of randomised controlled trials. BMJ 314: 1997, 1855-1859
38. Alderson P, Roberts I. Corticosteroids for acute traumatic brain injury. Cochrane Database Syst Rev. 2000; (2) CD000196
39. Edwards P, Arango M, Balica L et al: Final results of MRC CRASH, a randomised placebo-controlled trial of intravenous corticosteroid in adults with head injury-outcomes at six months. Lancet. 365(9475): Jun 4-10, 2005,1957-9.

Monitoring during Neurosurgery

Dr. P.K. Dash

Introduction

Neuroanaesthesia aims at providing ideal surgical condition and prevent neurological damage apart from standard anesthesia care. The host of surgical procedures performed warrants appropriate selection of monitoring methods. The neurological damages are mostly of ischemic origin and inevitable. They are related to the type of surgery, patient positioning, haemodynamic changes or any intercurrent event. New monitors are being introduced into the operating theatre, but only a few are considered to be an absolute standard of care in neurosurgery. In the past decade, new monitoring devices have moved from the experimental stage to the operating theatre and most are still in a phase of technological development The metabolic consequences of hyperventilation, pharmacological electroencephalogram burst suppression, hypothermia, etc. can now be assessed in the operating theatre. Non-invasive monitoring is being rapidly integrated into our daily work because of its lack of secondary effects. Nevertheless, each new development is regarded as an addition rather than as a substitute for existing equipment. The perfect combination of monitors to provide essential information during an individual surgical procedure to influence a better patient outcome is still uncertain and needs extensive clinical research. In the neuroanaesthesia curriculum the technical proficiencies related to monitoring include a)Insertion of arterial lines, b)Insertion of CVP lines, c)Techniques for detection and management of air embolism, d)EEG and evoked potentials techniques and e)Intracranial pressure measurement.

General monitoring

Routine monitoring needs attention for their merit, patient positioning and accessibility during surgery. They are ECG, SPO_2, NIBP, $ETCO_2$ and neuromuscular monitoring. In the absence of intracranial pressure monitoring it is safest to assume that any patient presenting with raised intracranial pressure still has a reduced intracranial compliance. Direct arterial pressure monitoring enables continuous monitoring of the CPP by transducing MAP at external

* Additional professor in Anaesthesiology, SSCTIMST, Trivandrum

auditory meatus. Arterial blood gas monitoring is superior to capnography for determining the accuracy of ventilation. Central venous cannulation provides hemodynamic monitoring and general vascular accesses. The blood glucose level is kept normal to minimize neuronal injury. Temperature monitoring facilitates controlled hypothermia and rewarming for cerebral protection. Continuous monitoring of raw or processed EEG (BIS or Entrppy) provides useful information on seizure activity and identifies burst suppression or isoelectric activity as well as depth of anaesthesia. Precordial Doppler, end tidal capnography and end tidal nitrogen monitoring are essential for detection of venous air embolism. In addition patient's medical condition and specific surgical needs dictate use of specific monitoring equipment.

Specific neurological monitoring

Intraoperative neuromonitoring is for detecting changes in the functional status of neronal tissue that is "at-risk" for intraoperative iatrogenic injury. The underlying premise of neuromonitoring is that impending neurologic injury is preceded by significant changes in neurologic activity or reduction in blood flow. They are classified into those that monitor intracranial pressure, blood flow dynamics and brain electrical activity. Intraoperative neuromonitoring promotes early warning of altered neural function thus enabling the surgeon to initiate propitious intervention to avoid postoperative impairment. Excess or accidental retraction of anatomic structures, compression or encroachment from bony structures or hematomas, mechanical stretching of the spinal cord, brainstem, cranial or peripheral nerves or disruption in cerebral, brainstem or spinal cord blood flow can all be detected early enough to allow prompt correction and reversal of neurologic compromise.

Intracranial pressure and blood flow dynamics monitors are

Intracranial Pressure Monitor

Jugular Venous Oximetry

Transcranial Doppler Sonography

Brain Tissue Oxygen Tension Monitor

Near-infrared Spectroscopy

Monitors of Brain Electrical Activity are

Electroencephalography

Evoked Potentials

Sensory Evoked Potentials

Visual

Somatosensory

Auditory

Motor Evoked Potentials

Intracranial pressure Monitoring

Normal Intracranial Pressure (ICP) is defined as the pressure inside the lateral ventricles or lumbar subarachnoid space in supine position. The normal value of ICP is 10-15 mm Hg in adults. It is 2-4 mmHg in neonates and infants. It reflects the relationship between intracranial contents and volume. Depletion of intracranial reserve volume for any reason leads to rapid rise in ICP. The purpose of ICP monitoring is to identify such increase and treat it before it causes cerebral ischaemia or herniation of the brain structures.

Indications

Head Injury provided the largest volume of data with ICP monitoring, though it has also been used in various other neurological conditions. They are Brain tumors, Subarchnoid hemorrhage, Hydrocephalus and medical conditions.

Head injury

About two thirds of patients with severe head injury have intracranial hypertension (ICP>20 mmHg). Aggressive maintenance of ICP at less than 15 mmHg has been suggested to improve the outcome. The recommendations of the Brain Trauma Foundation and American Association of Neurological Surgeons, for ICP monitoring, in head trauma include

1. Patients with severe head injury (GCS 3-8 after cardiopulmonary resuscitation) with an abnormal admission CT scan(one that shows haematomas, contusions, oedema, or compressed basal cisterns)
2. Patients with severe head injury with a normal CT scan if two or more of the following features are noted at admission
   a) age over 40 years,
   b) unilateral or bilateral motor posturing
   c) systolic blood pressure < 90 mmHg.
3. ICP monitoring is not routinely indicated in patients with mild or moderate head injury. However, a physician may prefer to monitor ICP in conscious patients with traumatic mass lesions such as haematomas and contusions.

Maintenance of Cerebral Perfusion Pressure (CPP) helps to avoid both global and regional ischaemia in brain trauma. A CPP of more than 70 mmHg need to be maintained in severe head injury. This can be effectively achieved only by concurrent measurement of ICP and systemic blood pressure.

Brain Tumors

The indications for ICP monitoring in patients with brain tumors are not clearly defined. Postoperative ICP monitoring is employed in patients with massive intraoperative brain swelling requiring aggressive treatments such as mechanical ventilation or barbiturate therapy and to diagnose postoperative haematoma in patients at higher risk like intraventricular tumors.

Subarachnoid haemorrhage

In patients with aneurysmal subarachnoid haemorrhage, ICP monitoring helps to diagnose occurrence of hydrocephalus and brain oedema due to cerebral vasospasm. In patients undergoing surgical or interventional neuroradological procedures for arteriovenous malformations, ICP monitoring helps in early detection of normal perfusion pressure breakthrough phenomenon, a complication that follows ablation of a high flow lesion.

Hydrocephalus and medical conditions

ICP monitoring establishes the need for CSF diversion procedures in patients with hydrocephalus when the indication for such an intervention is equivocal.

It is useful in Rye's syndrome, stroke, and encephalitis associated with raised ICP though the indications are not clearly defined.

Techniques of ICP monitoring

Following are the methods used with various advantages and disadvantages

1. Intraventricular Catheter
2. Intraparenchymal fiberoptic device
3. Subdural bolt
4. Epidural Device
5. Subdural catheter.

Intraventricular catheter

Intraventricular pressure monitoring is the gold standard against which all other ICP monitors are evaluated. The lateral ventricle is cannulated percutaneously by frontal, occipital, parieto-occipital or

parasagittal coronal approach and the cannula is connected to a pressure transducer through a fluid column. The transducer is calibrated at the level of the external auditory meatus.

The advantages of intraventricular monitoring are

a) it is reliable

b) it can be used for measurement of intracranial compliance

c) can also be used for draining CSF to reduce ICP

But, it is an invasive procedure associated with risks of infection and trauma to the brain during cannulation. Ventricular collapse in patients with brain oedema makes placement of the catheter difficult and interferes with actual pressure recordings.

Fiberoptic device

Small fiberoptic catheters are available that can be placed in the ventricles, epidural or subdural space or even in the brain parenchyma. Its main advantages are leaking, drift and infection are minimum since it is a self enclosed system.

The level of the transducer is of no concern as the transducer is at the tip

Subdural Bolt

It is a hollow bolt threaded through a twist drill hole into the skull and duramater until the inner surface of the bolt lies against the arachnoid mater. The bolt is connected to a pressure transducer via a saline column. The advantage of this system is that injury to the brain is remote. Its disadvantages include inability to draw CSF, infection, and malfunction if the bolt becomes loose or the brain matter protrudes into the hollow of the bolt.

Epidural and subdural catheters

They are easy to place but are less accurate than ventricular catheters

ICP waveforms

Under physiological conditions it is a pulsatile recording with slow respiratory component superimposed with cardiac cycle. Normally, respiratory oscillations are greater than the cardiac oscillations, but with raised arterial pulsations assume greater amplitude. Three pathological wave forms have been described in patients with raised ICP - Lundberg 'A', 'B and 'C' waves.

'A' waves

Also called as plateau waves, represent marked elevation of ICP caused by changes in regional cerebral blood volume (CBV). During these episodes, ICP rises to above 40 mmHg and is sustained at that level for 5-20 min. Initially, ICP returns to baseline level between two successive plateau waves, but progressively the baseline ICP also tends to rise. A plateau waves is associated with clinical deterioration. The patient complains of headache, loss of consciousness, or exhibit abnormal motor responses, breathing patterns and pupillary signs.

'B' waves

They have amplitude of about 20 mm Hg and occur at a rate of 1-2 per min. They act as warning signs of decreased intracranial compliance and enhanced risk of intracranial hypertension. 'B' waves, most often, occur synchronous with Cheyne-Stoke's breathing

'C' waves are not of any major pathological significance.

A change in ICP in response to a change in the volume of is a measure of intracranial elastance. The ICP change caused by addition of 1 ml of saline into the CSF space is a parameter that measures intracranial compliance and is known as Volume Pressure Ratio(VPR). A VPR of 4 mmHg or more indicates a gross decrease in intracranial compliance.

Pressure Volume Index (PVI) is another measure of intracranial compliance. PVI is calculated by the formula PVI = dV / Log (Pf/Pi) where dV is the change in the volume of the intracranial contents, Pi is the initial and Pf is the final ICP after addition of a known volume of CSF. A PVI less than 10 ml is associated with poor outcome.

Transcranial Doppler

Transcranial Doppler sonography is used to monitor blood flow velocity in major cerebral blood vessels. An examination carried out through the temporal window, orbital foramen or foramen magnum by using a 2 MHz probe provides clinically useful information with good correlation with the cerebral blood flow (CBF). Middle cerebral artery is commonly chosen for examination as it can be easily insolated and 75-80% of carotid blood flow, flows through MCA of the same side.

The velocities that are measured are the peak systolic, end-diastolic and mean velocity. Pulsatality index (PI) is a derived parameter calculated from the measured velocities.

PI = (Peak Systolic Velocity – End Diastolic Velocity) / Mean velocity

Interpretation and usefulness of TCD data

- Provided the vessel diameter is constant, a change in velocity is proportional to the change in flow or an increase or decrease of CBFV represents a similar change of CBF.

- When the insolated vessel diameter is not constant, a change in the velocity has no predictable relation to the CBF where it merely signifies a change in the diameter of the vessel.
- An increase in MCA blood flow velocity may indicate cerebral hyperemia or cerebral vasospasm. The distinction between the two can be made by hemispheric index. A value greater than 3 indicates cerebral vasospasm

  Hemispheric Index = VMCA / VICA (extracranial internal carotid artery flow)
- As the ICP increases, diastolic velocity decreases and the pulsatility increases. When the ICP is higher than the diastolic blood pressure but lower than the systolic blood pressure, a biphasic wave pattern results, followed by a total disappearance of the wave form when intracranial circulation stops.
- A good correlation exists between PI and ICP in head injury patients
- It is useful as a noninvasive monitor of CBF.
- It is helpful to monitor response to therapy in patients with subarachnoid haemorrhage and head injury.
- It is used to study autoregulation of CBF and cerebral vascular response to carbon dioxide.
- It can be used to assess intracranial circulatory status in raised ICP.
- It can be used to identify Intraoperative cerebral embolisation during surgery on carotid artery and cardiopulmonary bypass procedures.
- It can be used to optimise CPP and hyperventilation .

Jugular venous oximetry

Monitoring cerebral venous oxygen saturation as a measure of adequacy of CBF is based on the assumption that the product of CBF and arteriovenous oxygen content difference gives the cerebral metabolic rate of oxygen. Since arterial oxygen content varies very little over time in an individual with normal cardiorespiratory function, any decrease in CBF must be accompanied by a corresponding decrease in cerebral venous oxygen saturation if CMRO2 is constant.

A catheter placed into the jugular bulb retrogradely through internal jugular vein does monitoring of jugular venous oxygen saturation. For accurate measurement, the tip of the catheter must be within 1 cm of the jugular bulb otherwise contamination of the blood sample with venous drainage from extracranial veins gives inaccurate values. Once the catheter is in place, blood samples obtained intermittently and subjected to blood gas analysis. Alternatively, oximetric catheters may be used for continuous online measurement of SjVO2.

With the help of a jugular catheter it is possible to obtain at least three indices that are helpful in assessing the adequacy of CBF

1) jugular venous oxygen saturation ($SjVO_2$), normal 60 to 80%
2) cerebral arteriovenous oxygen difference(A-VDO), normal 5 to 7.5%
3) cerebral oxygen extraction (CEO_2) that is {SaO_2 - $SjVO_2$}, normal 24 - 40%.

A low $SjVO_2$, a high (A-V)DO_2 or a high CEO_2 indicates increased extraction of oxygen, which could bean early sign of cerebral ischaemia.

Clinical applications

- SjVO2 monitoring has been used to detect cerebral ischaemia during vascular neurosurgical and cardiopulmonary bypass procedures.
- Episodes of cerebral oxygen desaturation have been documented in about a third of patients with even normal CPP during craniotomy.
- In head injured patients, cerebral oxygen desaturation to less than 50% has been correlated with unfavorable outcome.
- SjVO2 monitoring can also be utilised to optimize the levels of CPP and hyperventilation in patients with cerebral pathology.

Limitations

The major limitation of SjVO2 monitoring is that it provides only a global estimate of the adequacy of CBF. A good correlation between SjVO2 and direct brain tissue oxygen tension is seen only in the normal areas of brain and not in areas with focal injury.

Brain tissue oxygen tension monitoring

Direct brain tissue oxygen tension (PbtO2) monitoring is currently under clinical investigation. A miniature Clarke's electrode incorporated into the tip of a catheter placed into the brain tissue through a twist drill hole. Early clinical studies indicate its usefulness in brain injury. Normal values for brain tissue oxygen tension are 20-40 mmHg. The risk of death increased significantly with the duration of PbtO2 values less than 15 mmHg and any occurrence of PbtO2 less than 6 mmHg. An SjVO2 value of 50% has been shown to correlate with a PbtO2 of 8.5 mmHg.

Near-infrared spectroscopy

- This system of monitoring used for quantification of cerebral blood flow, cerebral blood volume, regional cerebral oxygen saturation and cerebral metabolism.
- It is based on the principle of absorption of near-infrared light by chromophores in the body like oxyhaemoglobin, deoxyhaemoglobin and cytochrome aa3.
- By using light with different wave lengths, and applying suitable equations it simultaneously measures regional cerebral blood flow, cerebral blood volume, cerebral oxygen saturation and cerebral etabolism
- Presence of intracranial blood in the form of haematomas and contusions can interfere with the measurements.
- In adults, the currently available equipment seems to significantly underestimate CBF and CBV.

Electroencephalogram (EEG)

Electroencephalogram represents the electrical activity of the cerebral cortex. It represents the summation of the inhibitory and excitatory electrical potentials on the pyramidal cells. Surface or needle electrodes are used to record the electrical activity. The electrical potentials are recorded between any two chosen electrodes. For monitoring purposes recordings are made from multiple channels.

Interpretation of EEG

The amplitude of the normal EEG is 10-100 mV. Clinically, the EEG activity can be divided into four frequency bands: a - 8-13 Hz, b - 13-20 Hz, q - 4-8 Hz and d - 2-4 Hz. An isoelectric EEG represents total abolition of cortical electrical activity.

The methods of interpretation are

1. *Manual interpretation method*
2. *computer processing*
   a) time domain analysis
   b) frequency domain analysis.

Burst Suppression Ratio: This parameter represents the percentage of time the EEG is suppressed (isoelectric) in a given epoch.

Effects of anaesthetic agents on EEG

It is necessary to know the changes induced by anaesthetics from the pathological changes that may occur intra-operatively. In general an initial excitation resulting in a high frequency low amplitude activity followed by decrease in the frequency and increase in the amplitude, and finally, a decrease in both frequency and amplitude occurs at high doses.

Inhalational Anaesthetics

During induction,all of them cause loss of occipital activity and genesis of frontal activity. In surgical planes the anaesthetics differ in their effects on EEG.

- Isoflurane and desflurane at1.2 MAC cause burst suppression
- Enflurane causes spike seizure-like activity at 1.5 MAC
- Halothane causes linear slowing of frequency without burst suppression in clinical concentrations
- Nitrous oxide when used alone in subanaesthetic concentrations, causes fast rhythmic activity in frontal region
- When combined with volatile agents, it has been shown to antagonise or augment the EEG effects of volatile agents

Intravenous Anaesthetics

- Barbiturates at small doses cause drug-induced fast activity. In higher doses they cause EEG suppression and at very high doses cause burst suppression
- Methohexital enhances interictal epileptiform activity in patients with seizure disorder
- Etomidate and propofol cause myoclonic activity at induction
- Etomidate increases interictal epileptiform activity when used in small doses and causes burst suppression at high doses
- Propofol in anaesthetic doses may increaseor decrease interictal epileptiform activity. High doses of propofol cause burst suppression.
- Ketamine causes high amplitude theta activity and a significant increase in beta activity. Seizures may be caused in epileptic patients

ECG changes during cerebral ischemia

- Under stable anaesthetic conditions, any change in EEG may represent cerebral ischaemia and hypoxia.
- Slowing and flattening of EEG progressing to isoelectricity are the characteristic changes seen during ischaemia.
- Loss of slow activity may be one of the earliest signs of ischaemia.
- Seizure activity could be another manifestation of cerebral ischaemia.

- Ischaemic changes occur at different CBF with different anaesthetics.

Clinical applications of EEG

1. 16-channel EEG has been shown to be as sensitive as direct CBF measurement intraoperatively during carotid endarterectomy.
2. I ntraoperative EEG monitoring could be helpful to identify cerebral ischaemia during procedures associated with temporary vessel occlusion and during CPB
3. In the ICU, EEG monitoring detects seizure activity in patients with status epilepticus under the effect of muscle relaxants.
4. EEG is used to predict outcome of coma. It is also a tool for confirmation of brain death.
5. Various mathematical measures like median frequency, spectral edge frequency, bispectral index and entropy have been used for their potential to quantify the depth of anaesthesia

Evoked potentials

- Evoked potentials are the electrical responses generated in the nervous system in response to a stimulus.
- After appropriate stimulation, the responses are recorded from surface electrodes placed on scalp, spine or in the epidural space depending on the modality of the evoked potential used and the clinical requirement.
- Evoked potentials are event-related and pathway-specific.
- They have much lower amplitude than the normal EEG activity.hence they are very difficult to record and require computer averaging techniques to eliminate noise from the signal.
- Evoked potentials in clinical use can be
  - Sensory evoked potentials
  - Motor evoked potentials.

Sensory evoked potentials

They are the electrical potentials generated in response to stimulation of a peripheral sensory nerve. The modalities of evoked potentials are named after the sensory fibres stimulated

- Somatosensory evoked potentials (SSEP) are obtained by stimulation of somatic sensory nerve fibres
- Visual evoked potentials (VEP) by stimulation of visual pathways
- Auditory evoked potentials (AEP) by auditory pathway stimulation.

Once the nerves are stimulated, the responses are generally recorded from the scalp by surface electrodes or any point along the pathway of transmission of the nerve impulse.

Interpretation of an evoked potential recording consists of identification of specific peaks representing specific neural originators. Quantification of the latencies and amplitudes of the individual peak changes indicate injury to their corresponding neural originators. The electrical potentials in a given record are arbitrarily classified into three categories based on their latencies

- up to 10-40 msec after stimulus are called Short Latency Potentials
- from 20 to 120 msec are termed Intermediate Latency Potentials
- occurring after 120 msecare referred to as Long Latency potentials

Short latency potentials arise from subcortical structures, intermediate and long latency potentials arise from cerebral cortex. short latency potentials are used to monitor structures such as cranial or peripheral nerves, spinal cord and brain stem while long and intermediate latency potentials are used to monitor cerebral cortex.

Somatosensory Evoked Potentials

These potentials are obtained by applying electrical stimulus to the ulnar, median or posterior tibial nerves. Responses are recorded from electrodes placed on scalp or over the spine. Epidural electrodes are used intraoperatively.

Visual Evoked Potentials: Visual evoked potentials are generated in response to light stimulation of the retina by flashes of light from light-emitting diodes.

Auditory Evoked Potentials: Auditory evoked potentials are generated in response to stimulation of the tympanic membrane by audible short clicks

Effect of physiologic variables

A number of physiological parameters can affect the latencies and the amplitudes of the various peaks in evoked potential recordings

- Cerebral Blood Flow: Sensory evoked potentials are normal upto a CBF value of 20 ml/100g/minute. They start dropping when CBF decreases to 18-13 ml/100g/min. Evoked potentials cannot be obtained when CBF is below 10-12 ml/100 g/min
- Systemic Blood Pressure: Hypotension prolongs the conduction in the central nervous system thereby increasing the latencies of various peaks.

- Intracranial Pressure:Raised ICP result in an increase in the latency and a decrease in the amplitude of cortical potentials of VEP, AEP, and SSEP
- Deterioration of evoked potentials occurs when PaO2 is less than 40 mmHg.
- Latencies of VEP and SSEP are increased at a haematoctrit of 10-15%. Their amplitude is decreased when the haematoctrit is less than 10%.
- Extreme hypocapnia (PaCO2 < 25 mmHg) causes deterioration of eps
- Hypothermia increases the latency, reliable evoked potential recording is not possible at temperatures below 18 degree Celsius.

Effect of Anaesthesia

- Most anaesthetics decrease the amplitude and increase the latencies of the various peaks.
- Cortical potentials are affected more than the subcortical potentials.
- Brainstem and spinal potentials are least affected.
- The effects of anaesthetics on evoked potentials are dose-related; low concentrations of anaesthetics are compatible with reliable evoked potential recording.
- Inhalational anaesthetics vary in their potential to depress evoked potentials (N2O >Isoflurane > halothane).
- Thiopentone has no effect on brainstem potentials; however it depresses the cortical potentials which recover in 15-20 min.
- Etomidate has no effect on brainstem potentials while it *enhances* the cortical potentials.
- Propofol has no effect on spinal potentials. It depresses cortical components of auditory and somatosensory evoked potentials;
- Opioids and ketamine have no effect
- Benzodiazepines may exert little effect

Motor evoked potentials

Motor tract function monitoring is ideal during spinal procedures. Evoked responses generated by stimulation of the motor cortex have been used for this purpose. The stimulation may be transcranial electric motor evoked potentials (tcEMEP) or transcranial magnetic motor evoked potentials (tcMMEP).

The wave of depolarisation generated by the stimulation of corticospinal neurons descends through the corticospinal tracts and causes compound muscle action Potentials (CAMP). Responses to transcranial stimulation can be recorded in the epidural space, over the peripheral nerves or from evoked muscle activity.

Anaesthetics may have significant effects on motor evoked responses. Even low concentrations of inhalational anaesthetics may depress CMAP recording while epidural recording is not affected by even high concentrations of inhalational anaesthetics

- Thiopentone and midazolam produce CMAP depression that lasts for as long as 45 min after a bolus injection, making these agents less desirable.
- Propofol has been successfully used for epidural recording while CMAP recordings were depressed.
- Etomidate, ketamine and opioids are popular agents for CMAP recording
- Muscle relaxants may be helpful to reduce muscle artifact during epidural recording and strict control of muscle relaxation is necessary during recording of CMAP

Clinical applications of evoked potentials

- Evoked potentials are the only objective quantifiable measures of neurological function.
- Useful for the diagnosis of neurological conditions such as acoustic neuromas (brainstem auditory evoked responses, BAER) and multiple sclerosis (VEP).
- They have been used to assess the integrity of neural tracts when clinical examination is not feasible because of unconsciousness.
- SSEP and BAER have been extensively investigated in head injured patients to monitor for neurological deterioration, to assess the efficacy of therapeutic interventions, to determine prognosis and to diagnose braindeath.
- SSEP have been used extensively in prognostication of spinal injuries. Complete absence of SSEP is reliably followed by no recovery
- Intraoperative evoked potential monitoring has been successfully used in many neurosurgical operations.

  Some of the common conditions in which they are employed are
- Brain Stem Lesions (SSEP, BAER)
- Cerebellopontine Lesions (SSEP, BAER)
- Posterior Circulation Aneurysms (SSEP, BAER)

- Pituitary Lesions (VEP)
- Carotid Endarterectomy (SSEP, VEP)
- Cardiopulmonary Bypass (SSEP, VEP)
- Spinal Arteriovenous Malformations (SSEP)
- Scoliosis Surgery (SSEP)
- Stabilisation of Spinal Fractures (SSEP)
- Spinal Tumours (SSEP)
- Syringomyelia (SSEP)

Facial nerve monitoring

- Frequent involvement of facial nerve in cerebellopontine angle tumours has necessitated development of techniques for intraoperative monitoring of facial nerve function.
- Initial monitoring was facial nerve stimulation in the operative field and visual detection of the facial muscle activity.
- Current methods use recording of electromyogram of specific muscles like orbicularis oculi after stimulating the nerve in the operative filed. The signal is displayed on an oscilloscope and an audible confirmation of EMG is also provided.
- Several studies reported improved outcome in posterior fossa surgery with this monitor

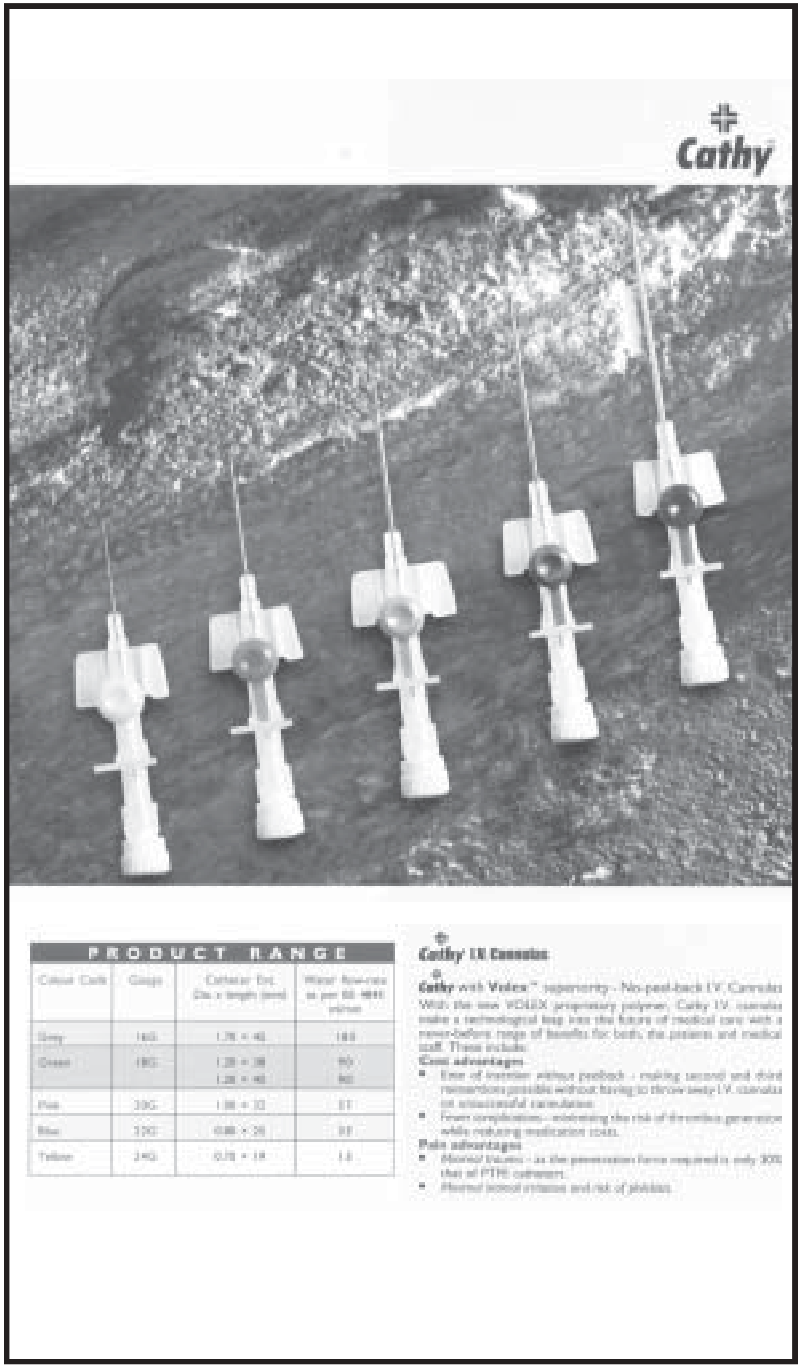
Conclusion

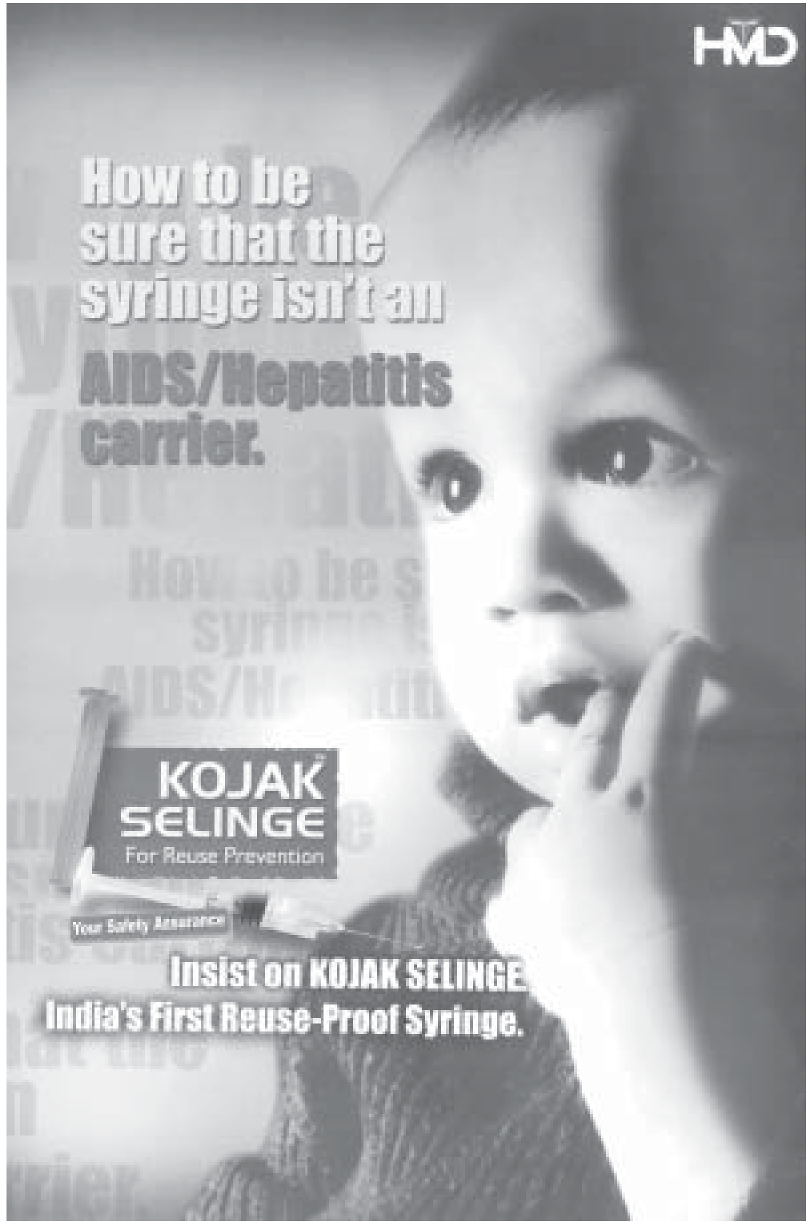
Selection of Intraoperative monitors used during neurosurgery is purely based on needs of the surgical condition. Among others, availability of equipment and technical expertise will bring down operative morbity when used widely.

Suggested reading:

Neurological monitoring, G. S. Umamaheswara Rao

Indian J. Anaesthesia. 2002; 46 (4) : 304-314


Cathy
PRODUCT RANGE
Cost advantages
Pain advantages


HMD
How to be sure that the syringe isn't an
AIDS/Hepatitis carrier.
KOJAK SELINGE
For Reuse Prevention
Your Safety Assurance
Insist on KOJAK SELINGE.
India's First Reuse-Proof Syringe.

Anaesthesia for Intra Cranial Tumors

Dr. Kurian P Thomas

Anaesthesia for intra cranial tumors have special considerations in view of raised Intra Cranial Pressure (ICP), high vascularity of brain leading to increased chance of bleding and relative less tolerance to the interruption of substrate delivery. In addition, the effect of tumors, anaesthetic and physiological factors controlled by anaesthesiologist do have an impact on brain homeostasis. Understanding these effects and tailoring the anaesthesia to the individual requirement is the main cornerstone of management of patients during surgery.

Effect of tumors on brain homeostasis

Most of us are well aware of the effect of intracranial space occupying lesion. The severity of symptoms depends upon the location of the tumor and rapidity of its growth. Tumors near the vital functional areas like motor cortex will have early manifestations whereas relatively silent areas like frontal lobe tumor present late. Similarly, rapidly growing tumors present early.

Since the cranium is incompressible, an increase in any of the three components (brain, blood, CSF) causes a compensatory decrease or displacement of other components- Munro kellie doctrine. This compensatory effect; over a period of time becomes ineffective thus resulting in an elevation of ICP. It may further be increased by the obstruction of CSF drainage by the tumor leading to hydrocephalous. Significant increase in ICP results in cerebral ischemia and herniation. Cerebral perfusion pressure is determined by Mean Arterial Pressure (MAP) and ICP; therefore any increase in ICP more than Mean Arterial Pressure (MAP) will produce cerebral ischemia. Increased ICP can produce herniation of brain across the meninges, down the spinal cord or through craniotomy, which leads on to neurological deterioration and death.

More over, these tumors produce functional impairment depending on the site of lesion due to mechanical compression of functional areas. To make things worse, the vasogenic oedemas in the surrounding areas further increase the mechanical effect. It is said that these lesions produces alteration in metabolism locally evidenced by changes in concentration of glucose, lactate etc.

Amrita Institute of Medical Sciences, Kochi.

The posterior fossa tumors, due to its close proximity to thevital centres may present with variety of problems. Haemodynamic variations in perioperative period are very common. Most of the lower cranial nerves traverse this space. So compression and damage to these nerves are common. This is important to anaesthesiologist as it can produce cardio respiratory compromise and difficulty in manging the airway by the patient.

Tumor resection under anaesthesia

Goals of anaesthesia:

The aims of anaesthesiologist during craniotomy are

- To maintain haemodynamic stability and cerebral perfusion pressure
- Avoidance of agents and techniques that increases the ICP
- Produce a slack brain that facilitates surgical retraction
- Planning for smooth and rapid awakening for early neurological assessment

Preoperative valuation

Evaluation is just like any other patient. It is important to do a baseline neurological evaluation. The aim of this is to know the degree of ICP raised; the degree of impairment of intra cranial compliance and auto regulation and the reserve available for ICP and cerebral blood flow before brain ischemia and neurologic impairment occurs. So a careful history and clinical evaluation is needed and recorded. Elucidating treatment history and its duration is also essential because some of these medications can alter intracranial compliance as well as pharmacokinetics and dynamics of anaesthetic drugs.

A thorough evaluation of patients' general condition with special emphasis to cardiovascular and respiratory status is needed. Posterior cranial fossa tumors present with lower cranial nerve palsies and history of recurrent aspiration. In adition, as these are in close proximity to brainstem, detrimental effect on cardiorespiratory function can occur. Further problem includes paraneoplastic syndromes and associated haematologic anomalies.

Laboratory evaluation is similar to any major cases. Preoperative diagnostic tests like CT, MRI etc should be checked to asses the lesion and its effect on homeostasis. Lastly a discussion with the surgeon is needed regarding the procedure, approach and position.

Premedication

All patients should receive stress ulcer prophylaxis. Antiepileptics and steroids should be continued. Sedative premedications should be avoided in sick patients with raised ICP, but mild sedatives like benzodiazepenes can be considered in small tumors. It is better to give some form of sedation under supervision once the patient is inside operation room to alleviate anxiety during attaching monitors and getting vascular access.

Monitoring

For most craniotomies, monitoring consists of standard monitors in addition to an intrarterial catheter. The invasive blood pressure monitoring is needed for strict control of blood pressure. Central Venous Pressure (CVP) monitoring is not routinely needed for tumor surgeries unless the case is expected to be long or if vascular haemorrhage is anticipated. CVP may be valuable in posterior cranial fossa surgeries especially in sitting position where air embolism is a complication. It may be helpful in procedure in which multiple infusions are used to facilitate intraoperative monitoring. Otherwise indications for pulmonary artery catheter and CVP remain same as for other patient population dictated by cardiac renal and pulmonary status.

Routine use of introperative electro physiologic monitors is not practiced. When these monitors are used anaesthesia should be tailored such a way that minimum interference is there.

Anaesthetic procedure

The major worrying factor during induction and intubation is an increase in ICP secondary to increase in blood pressure. So adequate depth of anaesthesia should be established before intubation. In addition, use of inhalational agents can produce an increase in ICP, which will be counteracted by elective hyperventilation. All induction agents can be used except ketamine. Fentanyl in the dose of 1-2 mg/kg or any other short acting opioids can be used to deepen the anaesthesia. Non-depolarizing muscle relaxants are preferred for intubation. Ventilation is controlled to achieve a PaCO2 around 30-35. Oxygen Nitrous oxide – inhalational agents (Isoflurane/Sevoflurane) or TIVA with propofol opioids can be considered. Another small dose short acting opioids can be given along with IV lignocaine 1-1.5 mg/kg, to suppress the haemodynamic response during intubation. Endotracheal tube should be secured properly as there is no access to airway once surgery begins. Flexometallic tube will be the choice in positions other than supine.

Skull pin application is another potential stimuli, which increases the blood pressure. This can be blunted by prior local infiltration, skull block or supplemental dose of opioids. During positioning anaesthesiologist should ensure that there is no impedance to venous return due to extreme kinking of venous channels. Padding and other care should be given to prevent inadvertent injuries due to prolonged positions.

Head up position, osmotic diuretics like mannitol during bone flap removal will further reduce ICP and help surgeon in retracting the brain.

There has been long standing controversy regarding the use of inhalational agents/intravenous agents for maintenance of anaesthesia. But till now no comparative study is available. The advantage of volatile agents is controllability, predictability and attainability of early awakening. However, it can increase cerebral blood flow, ICP and brain bulk. On the other hand, intra venous agents offer good control over cerebral blood flow, ICP and brain bulk. But prolonged or unpredictable awakening is the main concern. Current strategy is to use intravenous technique for high risk or complicated neurosurgical patients (high risk of ICP and cerebral ischemia) and volatile agents in uncomplicated cases.

Intraoperative increase in ICP should be managed by transient hyperventilation to reduce PaCO2, CSF drainage, deepening of anaesthesia with intravenous agents, use of diuretics etc.

Euvolemia is maintained intraoperatively. Preloading with fluids should be considered to prevent haemodynamic instability during induction. Hyperglycemia that worsens the consequences of ischemia and hypo osmolarity, which increases brain oedema, should be avoided. So it is better to avoid dextrose containing solutions and hypo osmolar solutions like Ringer's lactate.

Emergence from anaesthesia has respiratory cardiovascular and neurological consequences. The goals of emergence are predictable recovery to allow testing in the context of control haemodynmics and airway. In the early postoperative period, auto regulation is impaired. 20% develop an increase in ICP. Central drive of respiration and airway control is impaired. Awakening and extubation are associated with haemodynamic arousal. This can be partly abolished by intravenous beta-blockers or labetalol or lignocaine.

After extubation intracranial and extracranial homeostasis should be maintained. Ideally patient recovering should permit immediate assessment. But there are still some categories of patient in which early emergence is not appropriate. If the patient was suffering from obtunded consciousness or inadequate airway control preoperatively this problem is not likely to improve post op, making successful extubation unlikely. If there is risk of brain oedema, raised ICP or deranged intra cerebral haemostasis or homeostasis, ventilation is needed.

II. Awake craniotomy

Awake craniotomy allows cortical; mapping with patient cooperation. It helps to prevent neurological dysfunction during brain tumor resection. Despite widespread use of this technique its optimal management remains a challenge. It requires adequate depth of anaesthesia for craniotomy; which should be immediately followed by clear consciousness for cortical mapping. During this dramatic change in conscious level patient must be kept immobile and comfortable while respiration is maintained.

Advantages of awake craniotomy

- Opportunities to brain mapping allows maximal tumor resection, minimizing postoperative neurologic deficits.
- Avoidance of GA, hence the need for invasive monitoring
- Low complication rate and reduction in resource utilization

Preoperative evaluation and premedication

The decision to do awake craniotomy should be made by both the anaesthesiologist and the surgeon taking into consideration the patient factors. Most of the associated medical conditions are found to be only relatively contraindicated; a motivated patient with an uncomplicated airway and good psychological profile can be considered. The patient should be well informed about the procedure; its advantages and disadvantages. Careful attention should be paid to patient positioning and the degree of comfort.

Intraoperative management

Adequate analgesia and sedation are required till opening of dura and also during closure. During brain mapping and tumor resection patient should be fully conscious and cooperative to enable neurologic assessment. Several different sedation techniques and airway management during sedation have been tried. Sedation technique include neuroleptanalgesia, propofol with or without opioids, midazolam with opoids etc. These patients require local infiltration or skull block with bupivacaine is needed for skull frame application. Airway management with LMA, non-invasive ventilation have been tried.

All awake craniotomies carry the risk of respiratory depression and poor patient cooperation. Complication such as seizures, increased ICP, hypertension, nausea and vomiting can occur. So all antihypertensives antiepileptics should be continued. Constant vigilance and monitoring is needed during awake procedure.

III. Neuro navigation/ computer assisted surgery

It allows precise anatomical location and orientation before and throughout the surgical procedure. Image guided surgery can be preformed with the help of an MRI in the operating room or by feeding the data to the computer before surgery.

The anaesthetic requirement is same as any neurosurgical case.

Summary

There are several challenges in anaesthetizing a patient for tumor resection. The patient population ranges from small tumors with no change in ICP to large tumors with raised ICP and altered auto regulation. Surgical requirement in each surgery varies. Tailoring anaesthesia depending upon the patient demands and surgical requirements is an art and also it requires thorough understanding of cerebral homeostasis. Appropriate selection of anaesthetics and monitoring with meticulous general management of cardiorespiraory status, fluid replacement and positioning are all essential in improving the outcome.

References:

1. D S Smith,Irene Osborn. Posterior fossa anaesthetic considerations. In: Anaesthesia and Neurosurgery. Cottrell JE and Smith DS (ed) 4th ed. Mosby, Philadelphia: 2001, 335-348.
2. P Ravussin, O H G Widersmith.Supratentorial masses Anaesthetic considerations In: Anaesthesia and Neurosurgery. Cottrell JE and Smith DS (ed) 4th ed. Mosby, Philadelphia: 2001, 297-314.
3. Audree A Bendo. Supra tentorial tumors Evolving management and technique. In: 56th Annual Refresher course lectures and Basic science review 115-116
4. R F Cuchiara, S Black. Tumor surgery In: Clinical neuro anaesthesia. R F Cuchiara, S Black(ed) 2nd ed. 343- 388
5. Stoelting, Dierdorf. Diseases of nervous system In: Anaesthesia and Coexisting diseases. Stoelting, Dierdorf(ed) 233-245.
6. J C Drummond,P M Patel. Neurosurgical anaesthesia In: Anesthesia RD Miller (ed) 1895-1913
7. F Yammoto et al. Anesthesia for awke craniotomy with non invasive positive pressure ventilation. British Journal of Anaesthesia2003; 90: 382-5

Anesthesia for Neurosurgical Management of Intracranial Vascular Lesions

Dr. P. Gayatri, MD, FRCA

Intracranial vascular lesions include aneurysms, cavernomas, venous angiomas , dural fistulae and arteriovenous malformations. Here, we shall discuss the anesthetic management of patients undergoing neurosurgical procedures for intracranial aneurysms and cerebral arterio venous malformations (AVM).

Cerebral Aneurysms

Intracranial vascular surgery for clipping of the aneurysm poses special challenges to the anesthesiologist.

Patients with subarachanoid hemorrhage (SAH) from ruptured intracranial aneurysms have multiple organ dysfunctions and require careful evaluation.

Major causes of morbidity and mortality from SAH are:

- Direct effects of initial bleeding
- Delayed ischemic effects associated with vasospasm
- Rebleeding
- Surgical complications and
- Medical complications

Pathophysiology of SAH:

Thorough knowledge of the pathophysiological changes in the patient is important so that anesthesia can be tailored accordingly.

Neurologic effects:

Immediate

- Increased intracranial pressure (ICP)
- Acute hydrocephalus due to block of reabsorption of CSF by the hemorrhage
- Cerebral ischemia and infarction secondary to an acute increase in ICP
- Loss of auto regulation

Assistant Professor, Dept. of Anaesthesiology, SCTIMST, Trivandrum

Delayed

- Vasospasm-
  - Refers to vaso constriction of the large conducting arteries of the Circle of Willis.
  - Onset 3-4 days after SAH and peaks at 7 days.
  - Can result in cerebral ischemia, infarction and death and is a leading cause of morbidity and mortality after SAH.[1]
  - 20-46% of patients have symptomatic vasospasm.[1-4]
  - Break down product of RBC such as Oxyhemoglobin is thought to be the initiating agent.
  - Prophylactic nimodipine decreases the incidence of cerebral infarction as it is thought to improve the microcirculation after SAH. It does not however, alter the diameter of the vasospstic arteries.[5]
  - Early operation within 3 days of SAH in grade 2 and 3 patients has shown reduced incidence of vasospasm.[6]
  - Pre operative optimization of moderate to severe vasospasm may include-a). Hypervolemic and hemodilution therapy to improve CBF. Once the aneurysm is secured, hypertension is allowed, but there is no agreement on the range.[2] b). Transluminal angioplasty of major vessels c) Selective papaverine infusion of distal arterial vessels.
  - Other treatment modalities which are emerging include- intrathecal sodium nitroprusside infusion[7], tirilazad mesylate.[8]
  - Chronic Hydrocephalus- may require CSF diversion and
  - Rebleeding

Neurologic status:

· Generally graded using Hunt and Hess scale or the World Federation of Neurosurgical societies system (WFNS)

WFNS Grade	Glasgow Coma Score	Motor Deficit
1	15	Absent
2	14-13	Absent
3	14-13	Present
4	12-7	Present or absent
5	6-3	Present or absent

- Presence of cranial nerve deficits should be examined for even though it does not affect neurologic grading
- Patients with grade 4 and 5 will generally require postoperative ventilatory support due to decreased mental status, inability to protect the airway and cerebral swelling.
- Patients in grade 3 frequently require ventilatory support
- Patients in grade 1 and 2 can be extubated at the end of operation provided the intraoperative course is uneventful.

Cerebral blood flow:

Increased intracranial pressure (ICP) leads to a decrease in Cerebral Perfusion pressure (CPP). This results in reflex (Cushing's) increase in mean arterial Pressure (MAP) and cerebral vasodilation to maintain constant cerebral blood flow (CBF). The increase in cerebral blood volume leads to further increase in ICP. This cycle continues resulting in severe elevation of MAP with or without bradycardia.

Transmural pressure (TMP) in the aneurysm and the CPP are defined by the same equation i.e. MAP- ICP. Therefore as the risk of aneurysm rupture decrease with either a lower MAP or higher ICP, the risk of ischemia increases. Auto regulation i.e. the ability to maintain a constant CBF over a wide range of systemic pressures is defective or lost in patients with SAH and therefore the MAP should be maintained as close as possible to preoperative levels. [9-11]

Cardiovascular effects:

- Electro cardio graphic (ECG) abnormalities are found in up to 40-91% of SAH patients.[12]May persist for up to 10 days to 6 weeks
- Ventricular ectopics are the most common.
- Prolonged QTc and hypokalemia are associated with life threatening ventricular arrhythmias [12]
- Inverted T waves, ST segment depression, and U waves are commonly seen after SAH and do not necessarily indicate myocardial ischemia and dysfunction.
- Most of these changes are benign and considered neurogenic in origin due to the intense catecholamines surge, which may damage the heart by a prolonged increase in after load or by direct tissue toxicity.
- Cardiac troponin I (cTnI) assay is useful in detecting myocardial dysfunction.[1]Elevated levels are often found in poor grade SAH patients.
- Rarely, patients may suffer a myocardial infarct after an SAH because of a preexisting coronary artery disease.

- Aneurysm treatment should proceed as early as possible and not deferred in these patients to prevent rebleeding and cerebral ischemia.
- Death from cardiac cause after SAH is extremely low.[1]
- The presence of ECG changes does not appear to affect surgical outcome.

Pulmonary Complications:

- Is the leading non neurologic cause of death after SAH.[1]
- Pulmonary edema, pneumonia, and atelectasis are the most common pulmonary complications
- Pneumonia, pulmonary embolism and adult respiratory distress syndrome are the common cause of mortality.
- Pulmonary edema correlates with SAH grading. Occurs within the first week after SAH and peaks on 3 to 7 days.
- Pneumonia occurs because of a) aspiration during depressed mental status b) prolonged ventilation and c) prolonged bed rest predisposing to atelectasis and subsequent pneumonia. [1]

Fluid and electrolyte abnormalities:

- Dehydration is present in approximately 36-52% of SAH patients and correlates with the increasing grade of aneurysm.[14, 15]
- Hyponatremia is found with hypovolemia and is due to the release of brain natriuretic peptide.
- Both hypovolemia and hyponatremia are associated with increasesd incidence of cerebral ischemia and infarction [16,17]and hence should be avoided.
- Hypokalemia,hyperkalemia and hypernetremia can be seen.
- Hyper glycemia may occur and may worsen neurologic injury and hypovolemia.

Other Organs may be affected:

- Hepatic dysfunction
- Renal dysfunction
- Thrombocytopenia

Timing of surgery

- The risk of rebleeding during the first 24 hours after the initial bleed is 4% and 1.5% per day for the first 2 weeks.
- Improved outcome is seen in patients who underwent early surgery (0-3 days) after SAH.[18]

- Early operation (0-3days) reduces the risk of rebleeding, allows removal of subarachanoid blood (which reduces the incidence of vasospasm and infarction [19]), and permits liberal blood pressure management in patients who subsequently develop vasospasm.

Perioperative anesthetic goals:

The two most important goals are

- To minimize the risk of aneurysm rerupture by keeping the TMP low and
- Minimize cerebral ischemia by maintaining an adequate CPP (70-80 mm Hg).
- Because these two goals are governed by the same equation CPP or TMP = MAP- ICP, they work in opposition to each other.
- Patients in good grade tolerate a blood pressure reduction of about 25% without becoming ischemic as they have a normal ICP. Hyper ventilation does not benefit these groups of patients and may be harmful if it increases the TMP significantly.
- Patients in poor grade SAH do not tolerate hypotension. Hyperventilation may need to be instituted to lower ICP and to improve CPP but should be done gradually and cautiously to avoid re rupture. The $PaCO_2$ should be kept between 30-35 mm Hg. The reactivity to CO_2 is frequently lost in patients with vasospasm.[20-22]

Anesthetic management:

- Premedication for anxiety is usually omitted to avoid the risk of respiratory depression and CO_2 rise.
- Patients on ventilatory support are to be adequately sedated and paralyzed before shifting to avoid changes in blood pressure and ICP.
    - Nimodipine should be continued perioperatively
    - Dilantin should be maintained to decrease the incidence of seizures.

Intraoperative monitoring:

- Pulse oximetry, temperature, capnography and ECG (lead 2 and V5) are essential
- Direct intra-arterial blood pressure is imperative in all patients. Usually placed before induction in all patients (except in very anxious and unruptured aneurysm) as there is a significant risk of rerupture during laryngoscopy and intubation
- Central Venous Pressure (CVP) monitoring is desirable because a) of large changes in fluid shifts secondary to the use of diuretics b) possibility of cardiac dysfunction c) potential for large blood loss and d) high incidence of hypovolemia associated with SAH.
- Pulmonary artery catheter is indicated in poor grade patients with cardiac dysfunction.

Neurologic monitoring:

- Monitors of cerebral function (Electro encephalogram (EEG) and Somatosensory evoked potential (SSEP)) and monitors of CBF adequacy (jugular bulb catheter and trans cranial Doppler (TCD)) are useful.
- EEG and SSEP are of limited use because of signal attenuation and low sensitivity and specificity with general anesthesia. EEG is useful when burst suppression is desired. SSEP is not useful for posterior circulation aneurysm.
- Jugular bulb catheter monitors the cerebral venous oxygen saturation ($SjvO_2$). Reductions in $SjvO_2$ to less than 50 % suggest ischemia and needs to be treated with either an increase in oxygen delivery
    - by raising $PaCO_2$ thereby increasing CBF by producing vasodilation,
    - ensuring adequate oxygen saturation and a hematocrit greater than 30% and
    - increasing CPP by elevating the MAP with phenylephrine though done cautiously or a reduction in the cerebral metabolic demand
    - by lowering body temperature or
    - with intravenous anesthetics such as thiopentone.

Induction and tracheal intubation:

- The patient should be euvolemic before induction
- Thiopentone (3-5mg/kg) or propofol (2-3mg/kg) along with fentanyl (3-7 mg/kg) or sufentanyl (0.3-0.7 mg/kg) or remifentanyl (0.5mg/kg) can be used for induction. Muscle relaxants are used to aid intubation after allowing sufficient time for its effect.
- Careful monitoring of blood pressure is essential in this period. Esmolol and lignocaine can be used additionally to titrate the blood pressure. If the blood pressure rises by more than 20-30%, the procedure should be abandoned and anesthesia deepened.
- Periods of intense stimulation such as the application of head pins require additional deepening of anesthesia.

- Good communication between the surgeon and the anesthesiologist is required to prevent abrupt rises in blood pressure.

Positioning and maintenance of anesthesia:

- Proper positioning ensuring adequate venous drainage from the head is essential.
- Anesthesia can be maintained in good grade patients who are planned for extubation at the end can be maintained with short acting anesthetics. Nitrous oxide is a cerebral vasodilator when used in conjunction with a volatile anesthetic and should be used cautiously if at all.
- Neuromuscular blokade should be maintained intraoperatively except during monitoring of cranial nerve function with electromyography and brain stem monitoring using spontaneous breathing.

Fluid Management:

- Patient should be kept euvolemic before and slightly hypervolemic after clipping of the aneurysm. Hypo osmolar solutions such as lactated ringers are best avoided to reduce the development of cerebral edema. Measurement of blood loss and urine output along with CVP or Pulmonary artery pressure monitoring and should guide fluid management.
- Electrolytes and glucose should be monitored frequently.

Brain relaxation during surgery:

- ICP reduction should be done cautiously as it can cause a rise in TMP and re rupture of the aneurysm.
- The three brain compartments can be manipulated to reduce the brain volume during surgery i.e. brain bulk, Cerebrospinal fluid (CSF) and Cerebral Blood Volume (CBV).
- Mannitol with or without frusemide is used to decrease the brain bulk. Mannitol initially transiently increases CBF, CBV and ICP due to its high osmolarity. Patients with poor ventricular function may develop congestive cardiac failure and pulmonary edema. Rapid infusion can cause acute hypotension. Maximal effect is between 30-45 minutes. Therefore, it is usually started at skin incision and given over a period of 15-30 minutes.
- 20-30 ml of CSF can be drained through a lumbar drain or ventriculostomy to facilitate dural incision. Excess CSF drainage before dural opening should be avoided.

- CBV can be reduced with improved venous drainage, hypocapnia, and CMRO2 reduction.

Aneurysm Clipping:

- Induced or controlled hypotension is used to decrease aneurysm wall tension and facilitate clipping. It is contraindicated if vasospasm is present. Sodium nitroprusside and isoflurane are commonly used for this purpose. As both these agents also cause cerebral vasodilation they may not be useful if brain is not relaxed adequately.
- Use of adenosine to provide brief periods of asystole to facilitate aneurysm occlusion warrants evaluation.[23]
- Once the aneurysm is secured, hypertension is allowed, but there is no agreement on the range.[2]

Temporary Clipping:

- Involves occlusion of the parent vessel to prevent the risk of aneurysm rupture during dissection and clipping.
- Communication between the anesthesiologist and the surgeon is essential if temporary clipping is planned to maximize the cerebral protection and optimal blood pressure management.
- MAP should be maintained at mildly elevated levels to improve collateral flow.
- The risk of cerebral ischemia is less if temporary occlusion time is less than 10 minutes. Many studies have reported good outcomes with 20 minutes. [24,25] Longer than 20 minutes are associated with a grater incidence of postoperative cerebral infarction.[26]
- Pharmacological cerebral protection is practiced in some centers during temporary occlusion.
  - The ‘Sendai Cocktail’ (mannitol 2g/kg, dexamethasone 50 mg and vitamin E 500 mg) is used by some groups. Phenytoin has replaced dexamethasone in this cocktail.[27]
  - Burst suppression doses of etomidate (0.4-0.5 mg/kg), thiopentone (5-6 mg/kg), propofol (3-5 mg/kg) have also been used with or without mannitol. EEG monitoring can be useful in this situation. These agents should be carefully given as these agents also can cause systemic hypotension. If required blood pressure should be maintained with a vasopressor infusion such as phenylephrine.
  - Hypothermia was thought to confer additional protection by decreasing CMRO2 and glutamate release. But the IHAST 2 trial has found no benefit of hypothermia in good grade (1,2 and 3) patients undergoing surgical clipping.[28]

Intraoperative rupture of aneurysm:

- It is often associated with poor outcome.
- Incidence varies with the location and the size of aneurysm and the institution. The International Cooperative study on the timing of aneurysm surgery observed an incidence of 18% [29]
- The state of dissection and the aneurysm anatomy influences if control can be achieved quickly. If not, massive blood loss may ensue.
- Close attention and communication with the surgeon is needed during aneurysm dissection and occlusion.
- Blood pressure may have to be lowered briefly to 50 mm of Hg or less to facilitate surgical control. It is important to maintain normal blood volume while blood pressure is lowered.
- If time permits and the patient remains hemodynamically stable, then thiopental may be given for cerebral protection.

Emergence:

- Patients in good grade are allowed to wake up and extubated. During emergence blood pressure should be controlled to 30% of baseline using labetalol, esmolol or vasodilators such as SNP and NTG. However, vasodilators can increase ICP.
- Patients in grade 3-5 are electively ventilated in the postoperative period. Hypertensive, hypervolemic and hemodilution therapy is re instituted for vasospasm if present.

Hypothermic circulatory arrest for giant aneurysm:

- Used for giant aneurysms size >2.5 cm and complex vertebro basilar aneurysm as perforating vessels are often incorporated into the aneurysm neck, which is usually broad based. Temporary occlusion time of 10-20 minutes is insufficient to place a clip around the neck. Therefore these aneurysms are approached through the hypothermic circulatory arrest to collapse the aneurysm and identify the perforators.
- Mortality and morbidity is high.
- Hypothermia to 10-15 C provides cerebral protection and permits around 60 minutes of circulatory arrest. Barbiturates in this setting do not reduce CMRO2 further, but is thought to promote free radical scavenging and membrane stabilization.
- Hypothermia leads to decreased cardiac output and raised systemic vascular resistance. Vasodilators such as SNP are useful to promote rapid cooling.

- Atrial or ventricular fibrillation occurs at 28-30 C. VF should be treated with either cardioversion or 40-80 meq of potassium chloride to prevent cardiac ischemic injury.
- Hyperglycemia should be avoided.
- Bleeding is a major problem as coagulation system is affected.
- EEG is useful for monitoring burst suppression.

Reference

1. Solenski NJ, Haley EC Jr, Kassell NF, Kongable G, Germanson T, Truskowski L, Torner JC. Medical complications of aneurysmal subarachnoid hemorrhage: a report of the multicenter, cooperative aneurysm study. Participants of the MulticenterCooperative Aneurysm Study. Crit Care Med. 1995 Jun; 23(6): 1007-17.
2. Suarez JI, Tarr RW, Selman WR. Aneurysmal subarachnoid hemorrhage. N Engl J Med. 2006 Jan 26;354(4):387-96. Review
3. Charpentier C, Audibert G, Guillemin F, Civit T, Ducrocq X, Bracard S, Hepner H, Picard L, Laxenaire MC. Multivariate analysis of predictors of cerebral vasospasm occurrence after aneurysmal subarachnoid hemorrhage. Stroke. 1999 Jul; 30(7): 1402-8.
4. Rajendran JG, Lewis DH, Newell DW, Winn HR. Brain SPECT used to evaluate vasospasm after subarachnoid hemorrhage:correlation with angiography and transcranial Doppler. Clin Nucl Med. 2001 Feb; 26(2): 125-30.
5. Petruk KC, West M, Mohr G, Weir BK, Benoit BG, Gentili F, Disney LB, Khan MI, Grace M, Holness RO, et al. Nimodipine treatment in poor-grade aneurysm patients. Results of multicenter double-blind placebo-controlled trial.J Neurosurg. 1988 Apr; 68(4): 505-17.
6. Inagawa T. Effect of early operation on cerebral vasospasm. Surg Neurol. 1990 Apr; 33(4): 239-46.
7. Thomas JE, Rosenwasser RH, Armonda RA, Harrop J, Mitchell W, Galaria I. Safety of intrathecal sodium nitroprusside for the treatment and prevention of refractory cerebral vasospasm and ischemia in humans.Stroke. 1999 Jul; 30(7): 1409-16
8. Kassell NF, Haley EC Jr, Apperson-Hansen C, Alves WM. Randomized, double-blind, vehicle-controlled trial of tirilazad mesylate in patients with aneurismal subarachnoid hemorrhage: a cooperative study in Europe, Australia, and New Zealand.J Neurosurg. 1996 Feb; 84(2): 221-8.
9. Voldby B, Enevoldsen EM, Jensen FT. Cerebrovascular reactivity in patients with ruptured intracranial aneurysms.J Neurosurg. 1985 Jan; 62(1): 59-67.
10. Ma X, Willumsen L, Hauerberg J, Pedersen DB, Juhler M. Effects of graded hyperventilation on cerebral blood flow autoregulation in experimental subarachnoid hemorrhage.J Cereb Blood Flow Metab.

2000 Apr; 20(4): 718-25.

11. Handa Y, Hayashi M, Takeuchi H, Kubota T, Kobayashi H, Kawano H. Time course of the impairment of cerebral autoregulation during chronic cerebral vasospasm after subarachnoid hemorrhage in primates .J Neurosurg. 1992 Mar; 76(3): 493-501.
12. Andreoli A, di Pasquale G, Pinelli G, Grazi P, Tognetti F, Testa C. Subarachnoid hemorrhage: frequency and severity of cardiac arrhythmias. A survey of 70 cases studied in the acute phase. Stroke. 1987 May-Jun; 18(3): 558-64.
13. Parekh N, Venkatesh B, Cross D, Leditschke A, Atherton J, Miles W, Winning A, Clague A, Rickard C. Cardiac troponin I predicts myocardial dysfunction in aneurysmal subarachnoid hemorrhage. J Am Coll Cardiol. 2000 Oct; 36(4): 1328-35.
14. Nelson RJ, Roberts J, Rubin C, Walker V, Ackery DM, Pickard JD. Association of hypovolemia after subarachnoid hemorrhage with computed tomographic scan evidence of raised intracranial pressure. Neurosurgery. 1991 Aug; 29(2): 178-82. Erratum in: Neurosurgery 1991 Sep; 29(3): 479.
15. Wijdicks EF, Vermeulen M, ten Haaf JA, Hijdra A, Bakker WH, van Gijn J. Volume depletion and natriuresis in patients with a ruptured intracranial aneurysm. Ann Neurol. 1985 Aug; 18(2): 211-6.
16. Wijdicks EF, Vermeulen M, Hijdra A, van Gijn J. Hyponatremia and cerebral infarction in patients with ruptured intracranial aneurysms: is fluid restriction harmful? Ann Neurol. 1985 Feb; 17(2): 137-40.
17. Hasan D, Wijdicks EF, Vermeulen M. Hyponatremia is associated with cerebral ischemia in patients with aneurismal subarachnoid hemorrhage. Ann Neurol. 1990 Jan; 27 (1): 106-8.
18. Haley EC Jr, Kassell NF, Torner JC. The International Cooperative Study on the Timing of Aneurysm Surgery. The North Americanexperience.Stroke.1992Feb; 23(2): 205-14.
19. Taneda M. The significance of early operation in the management of ruptured intracranial aneurysms—an analysis of 251 cases hospitalized within 24 hours after subarachnoid haemorrhage. Acta Neurochir (Wien). 1982; 63(1-4): 201-8.
20. Hassler W, Chioffi F. CO2 reactivity of cerebral vasospasm after aneurysmal subarachnoid haemorrhage.Acta Neurochir (Wien). 1989; 98(3-4): 167-75.
21. Kamiya K, Kuyama H, Symon L. An experimental study of the acute stage of subarachnoid hemorrhage.J Neurosurg. 1983 Dec; 59(6): 917-24.

22. Mendelow AD, McCalden TA, Hattingh J, Coull A, Rosendorff C, Eidelman BH. Cerebrovascular reactivity and metabolism after subarachnoid hemorrhage in baboons. Stroke. 1981 Jan-Feb; 12(1): 58-65.
23. Groff MW, Adams DC, Kahn RA, Kumbar UM, Yang BY, Bederson JB. Adenosine-induced transient asystole for management of a basilar arteryaneurysm. Case report. J Neurosurg. 1999 Oct; 91(4): 687-90.
24. Lavine SD, Masri LS, Levy ML, Giannotta SL. Temporary occlusion of the middle cerebral artery in intracranial aneurysm surgery: time limitation and advantage of brain protection.J Neurosurg. 1997 Dec; 87(6): 817-24.
25. Ikawa F, Kiya K, Kitaoka T, Yuki K, Arita K, Kurisu K, Uozumi T. [Multivariate analysis of intentional temporary vessel occlusion in aneurismal surgery] No Shinkei Geka. 1998 Jan; 26(1): 19-24. Japanese.
26. Ogilvy CS, Carter BS, Kaplan S, Rich C, Crowell RM. Temporary vessel occlusion for aneurysm surgery: risk factors for stroke in patients protected by induced hypothermia and hypertension and intravenous mannitol administration. J Neurosurg. 1996 May; 84(5): 785-91.
27. Mizoi K, Yoshimoto T. Permissible temporary occlusion time in aneurysm surgery as evaluated by evoked potential monitoring. Neurosurgery. 1993 Sep; 33(3): 434-40; discussion 440
28. Todd MM, Hindman BJ, Clarke WR, Torner JC. Mild intraoperative hypothermia during surgery for intracranial aneurysm. N Engl J Med 2005; 352:135-145.
29. Kassell NF, Torner JC, Haley EC Jr, Jane JA, Adams HP, Kongable GL. The International Cooperative Study on the Timing of Aneurysm Surgery. Part 1: Overall management results. J Neurosurg. 1990 Jul; 73(1): 18-36.

Arterio Venous Malformations (AVM)

Cerebral AVMs are a complex tangle of thin-walled, abnormal vessels without an intervening capillary bed.[1] The tangle of vessels, termed the "nidus," acts as an arteriovenous shunt.

The malformations are presumed to be congenital lesions resulting from abnormal vascular formation during embryonic development.[2,3] They may exert a deleterious effect on brain function via several mechanisms, including mass effects (for example, hematoma, edema, or gradually expanding abnormal vascular structures such as venous aneurysms), metabolic depression (diaschisis), and seizure activity.

The most common presentation is spontaneous intracranial hemorrhage.

The primary goal of treatment is to decrease the risk of spontaneous bleeding. Intervention is undertaken with the goal of complete AVM obliteration, because subtotal therapy does not confer protection from hemorrhage.

Grading of AVM

Spetzler-Martin grading is generally followed. Grading is based on

- the size (<3 cm=1, 3-6 cm=2, >6 cm=3) ,
- location of the AVM in the eloquent area(no=0, yes=1) and
- the presence of deep draining veins (no=0,yes=1)

At present, there are 4 major treatment options available for patients with an AVM of the brain. Management strategies are based on the grading of the AVM and include single or combined therapy applying

- microsurgery,
- endovascular technique
- radiosurgery (focused radiation) and
- conservative management

Choice of treatment [4]

In general, surgical extirpation is strongly considered as the primary mode of therapy for Spetzler-Martin grade I and II lesions. For patients with small lesions, where surgery offers some increased risk based on location or feeding vessel anatomy, radiosurgery should be strongly considered.

For grade III lesions, a combined modality approach with embolization followed by surgery is often feasible .

Surgical treatment only is often not recommended for grade IV and V lesions because it confers a high risk.

Surgical perspective

Lesions are typically excised by standard microsurgical techniques with the operating microscope.

The arterial feeders are generally attacked first, followed by excision of the nidus of the lesion and finally resection of the draining vein.

In general, the veins are preserved until the very end of the operation to prevent intraoperative AVM rupture and hemorrhage.

Associated Aneurysms

Intracranial aneurysms are found in approximately 7 to 17% of patients with AVM.

Intracranial aneurysms can occur on the feeding artery to the AVM. These may involute after resection or obliteration of the brain AVM. Alternatively, patients may also harbor more saccular intracranial aneurysms at typical locations in the circle of Willis.

It is recommended that these be approached during the same surgery if the operative field is adequate or that they be treated separately with endovascular or open surgical obliteration.

Anesthetic consideration for the surgical management of the AVM:

Because AVM resection is usually not emergent, preexisting medical conditions should be optimized.

An important consideration throughout the operative period is the potential for massive, rapid, and persistent blood loss. Appropriate monitoring together with adequate amounts of blood, along with access for its administration, must be readily available.

The choice of anesthetic agent must be consistent with safe conduct of intracranial surgery.

The management goals should include

- ensuring brain relaxation,
- controlled systemic and cerebral hemodynamics,
- maintenance of isotonicity , euglycemia and normothermia, and
- a controlled emergence from the state of anesthesia.

Monitoring:

In addition to routine monitors central venous access or pulmonary artery catheter should be considered for resection of larger lesions, which may require either induced hypotension or massive volume therapy.

Transduction of vascular pressures in the operative field:

This may aid the surgeon in differentiating arterial and venous structures. In certain cases, it may assist in the decision of whether a draining vein that interferes with surgical access to the nidus can be sacrificed. Proximal arterial pressure is measured during a temporary occlusion of the vein; if the pressure does not change, this implies that alternate venous pathways are sufficient to prevent distention of the nidus and rupture.

Brain relaxation

- Proper positioning of the patient's head promoting intracranial venous drainage is necessary.
- Cerebral spinal fluid removal is an effective means of inducing brain relaxation and is obtained by direct lumbar puncture or ventricular drainage.
- Diuretic therapy with mannitol and/or furosemide is widely applied.
- The most important consideration for the choice of an intraoperative anesthetic is the avoidance of cerebral vasodilators.
- Modest hypocapnia should be applied sparingly as an adjuvant to brain relaxation, but levels below 30 mm Hg should have a specific indication.

Hemodynamic control

- Spontaneous hemorrhage during the perioperative period as a result of variations in systemic blood pressure is probably less likely because of a "buffering" capacity of the fistula on changes in systemic pressure.[5]
- Adequate preload should be maintained for the adequate control of systemic blood pressure. Iatrogenic dehydration, as practiced in years past, has no place in modern neurosurgical practice.
- Induced hypotension is frequently useful during AVM resection, especially in large AVMs that have a deep arterial supply. Bleeding from these small, deep-feeding vessels may be difficult to control, and decreasing arterial pressure facilitates surgical hemostasis. Choice of hypotensive agent must be placed in the context of the clinical situation (e.g., avoidance of beta-adrenergic blockers with bronchospastic airway disease or use of nitroglycerin with coronary artery disease) and the experience of the practitioner.
- During uncontrolled bleeding, the surgeons may be forced to place clips blindly in an attempt to stem the hemorrhage. In this event, barbiturate therapy may be indicated, and it could be used as a means of or as an adjuvant to the induction of mild or moderate temporary arterial blood pressure reduction until bleeding is controlled.

Fluid and electrolyte management

- Serum osmolality has to be maintained as it is the determinant of fluid movement into the damaged brain. Hypoosmolar solutions such as ringer's lactate has to be avoided.

- In the event of a hamorrhage, aggressive administration of only isotonic crystalloids without blood and colloids may worsen brain edema by decreasing colloid oncotic pressure.[6]
- Hyperglycemia has to be avoided as glucose aggravates cerebral injury.[7, 8]

Temperature Control

- Two randomized controlled clinical trials showed a favorable result of mild hypothermia in patients with severe traumatic brain injury.[9, 10]
- The efficacy of prophylactic mild hypothermia during craniotomy has been validated in the recent IHAST 2 (Intraoperative hypothermia during aneurysm surgery trial) in which application of hypothermia to good grade (grade 1-3) subarachanoid hemorrhage patients has not shown any benefit.[11]
- Pending further evidence, it would seem prudent to maintain normothermia in the intra operative period.

Emergence and Initial Recovery

A moderate blood pressure augmentation (20-30% above normal mean arterial pressure) may be needed at the time of hemostasis. After hemostasis is achieved and the volatile agent is discontinued, antihypertensive agents such as labetalol or esmolol can be used to maintain the patient's blood pressure within 10% below the baseline values.

Control of systemic hemodynamics is of critical importance during the emergence phase as the patient makes the transition from the anesthetized to the conscious state.

Perioperative complications

Brain Edema/Hemorrhage

Two hypotheses for the cause of brain edema and hemorrhage during or after surgery have been proposed: Normal Perfusion pressure breakthrough (NPPB) or occlusive hyperemia.

Normal perfusion pressure breakthrough is attributed to cerebral hyperemia caused by repressurization of previously hypotensive regions. This theory assumes that chronic dilation of vessels in hypotensive/ischemic territory leads to a loss of autoregulation.[12]

There are, however, several observations that contradict this theory[13-16] and an alternate hypothesis have been proposed regarding the cause of malignant postoperative edema and hemorrhage termed "occlusive hyperemia."

With regard to perioperative management, the diagnosis of NPPB should be one of exclusion after all other correctable causes for malignant brain swelling or bleeding have been excluded. In addition to other supportive and resuscitative measures, the prevention of severe postoperative hypertension may be useful in preventing and treating this syndrome.

Reference

1. Mandybur TI, Nazek M: Cerebral arteriovenous malformations. A detailed morphological and immunohistochemical study using actin. Arch Pathol Lab Med 114:970-973, 1990
2. Rothbart D, Awad IA, Lee J, et al: Expression of angiogenic factors and stuctural proteins in central nervous system vascular malformations. Neurosurgery 38:915-925, 1996
3. Sonstein WJ, Kader A, Michelsen WJ, et al: Expression of vascular endothelial growth factor in pediatric and adult cerebral arteriovenous malformations: an immunocytochemical study. J Neurosurg 85:838-845, 1996
4. Ogilvy CS, Stieg PE, Awad I, Brown RD Jr, Kondziolka D, Rosenwasser R, Young WL, Hademenos G; Special Writing Group of the Stroke Council, American Stroke Association. AHA Scientific Statement: Recommendations for the management of intracranial arteriovenous malformations: a statement for healthcare professionals from a special writing group of the Stroke Council, American Stroke Association.Stroke. 2001 Jun;32(6):1458-71.
5. Gao E, Young WL, Pile-Spellman J, et al: Cerebral arteriovenous malformation feeding artery aneurysms: a theoretical model of intravascular pressure changes after treatment. Neurosurgery 41:1345-1358, 1997
6. Drummond JC, Patel PM, Cole DJ, et al: The effect of the reduction of colloid oncotic pressure, with and without reduction of osmolality, on post-traumatic cerebral edema. Anesthesiology 88:993-1002, 1998
7. Kilic T, Pamir MN, Kullu S, et al: Expression of structural proteins and angiogenic factors in cerebrovascular anomalies. Neurosurgery 46:1179-1192, 2000
8. Lam AM, Winn HR, Cullen BF, et al: Hyperglycemia and neurological outcome in patients with head injury. J Neurosurg 75:545-551, 1991
9. Marion DW, Penrod LE, Kelsey SF, et al: Treatment of traumatic brain injury with moderate hypothermia. N Engl J Med 336:540-546, 1997
10. Clifton GL, Allen S, Barrodale P, et al: A phase II study of moderate hypothermia in severe brain injury. J Neurotrauma 10: 263-273, 1993
11. Todd MM, Hindman BJ, Clarke WR, Torner JC. Mild intraoperative hypothermia during surgery for intracranial aneurysm. N Engl J Med 2005; 352:135-145.

12. Spetzler RF, Wilson CB, Weinstein P, et al: Normal perfusion pressure breakthrough theory. Clin Neurosurg 25:651-672, 1978
13. Young WL, Kader A, Ornstein E, et al: Cerebral hyperemia after arteriovenous malformation resection is related to "breakthrough" complications but not to feeding artery pressure. The Columbia University Arteriovenous Malformation Study Project. Neurosurgery 38:1085-1095, 1996
14. Young WL, Kader A, Prohovnik I, et al: Pressure autoregulation is intact after arteriovenous malformation resection. Neurosurgery 32:491-497, 1993
15. Young WL, Pile-Spellman J, Prohovnik I, et al: Evidence for adaptive autoregulatory displacement in hypotensive cortical territories adjacent to arteriovenous malformations. Columbia University AVM Study Project. Neurosurgery 34:601-611, 1994
16. Young WL, Prohovnik I, Ornstein E, et al: The effect of arteriovenous malformation resection on cerebrovascular reactivity to carbon dioxide. Neurosurgery 27:257-267, 1990

Management of Patients with Head Injury presenting for Surgery

Dr. K.P. Unnikrishnan

Traumatic brain injury (TBI) is the leading cause of death in trauma victims, accounting for approximately half of all trauma-related deaths (1). Destruction of brain tissue during injury occurs in two phases: the primary injury, which involves direct tissue damage at the time of the inciting event, and the subsequent secondary injury, which occurs due to ischemia, causing calcium ion influx and free radical accumulation. Primary injury is considered irreversible, and therefore therapy is directed toward minimizing the secondary injury by optimizing cerebral perfusion pressure (CPP) and cerebral blood flow (CBF) and by aggressive treatment of intracranial hypertension. The ultimate goal in the management of patients with head injury is to reduce the mortality rate and to improve the functional status of those who survive. To achieve this, prevention of secondary injury to the already injured brain and aggressive management at three different levels is required: pre-hospital transportation, emergency room, and operating room/intensive care unit.

Pre-hospital resuscitation

The initial management of all trauma victims follows the ABCs of resuscitation: airway, breathing, and circulation. This approach is based on the identification of the sequential variables that could cause the victim's death:

A: airway with cervical spine control

B: breathing (hemo or pneumothorax)

C: circulation (maintenance of blood pressure, control of hemorrhage)

D: disability (Glasgow Coma Scale)

E: exposure (examination from head to toe)

S: secondary evaluation

* *Assistant professor, Department of Anaesthesiology, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum.*

Emergency room management of head injury

The Glasgow Coma Scale (GCS), described by Teasedale and Jennett(2), will allow to classify head injury victims in to:

13 – 15: Minor

9 – 12: Moderate

3 – 8: Severe

predictors of neurological outcome for patients with moderate and severe head injury include age, Glasgow coma scale score, and papillary reactivity (3)

Table 1. predictors of neurological outcome for patients with moderate and severe head injury

Predictors of complications

Patient age, GCS score, papillary reactivity

Predictors of death

Patient age, GCS score, pupillary reactivity, injury severity score, presence of hematoma on CT scan.

According to the severity patients are hospitalized in the general ward, in an Intermediate Care Unit or in the Intensive Care Unit. This also implied a therapeutic option: the less severe the lesion the less complexity in treatment, so in this manner patients with moderate head injury could be treated as minor or severe head injury, following different guidelines.

Severe head injury management has been outlined in different Guidelines (Brain Trauma Foundation (BTF) and European Brain Injury Consortium EBIC).These Guidelines were developed according to the standards of the evidence-based medicine with three levels of evidence:

Class I evidence (Standards):

Prospective randomized controlled trials, the gold standard of clinical trials. However some may be poorly designed, lack sufficient patient numbers or suffer from other methodological inadequacies.

Class II evidence (Guidelines):

Clinical studies in which the data was collected prospectively, and retrospective analyses that were based on clearly reliable data (observational, cohort, prevalence and case control studies).

Class III evidence (Options):

Most studies based on retrospectively collected data (clinical series, databases or registries, case reviews, case report) and Expert opinion.

The treatment strategies involved are:

1. Airway management
2. Resuscitation of oxygenation and blood pressure
3. Indications for intracranial pressure monitoring
4. Intracranial pressure treatment threshold
5. Recommendations for intracranial pressure monitoring technology
6. Guidelines for cerebral perfusion pressure
7. Hyperventilation
8. Use of Mannitol
9. Use of barbiturates in the control of intracranial hypertension
10. Role of steroids
11. Nutrition
12. Role of antiseizure prophylaxis following head injury

Airway management

In the multiply injured patients with a severe TBI, tracheal intubation must be established with in-line stabilization of the neck, due to an approximately 6% incidence of cervical spine injury associated with TBI (4). Conversely, approximately one quarter to one third of patients with cervical spine and /or spinal cord injuries have been found to have moderate to severe head injuries (4, 5). The stabilization of the neck until x-rays can demonstrate absence of a cervical spine fracture is important for all severely head-injured patients. A quick neurological examination before administration of muscle relaxants and /or sedative drugs is beneficial in determining the initial extent of brain or spinal cord injuries and in the prognostication.

The airway may be difficult to secure due to associated facial fractures, blood and vomitus in the oral cavity. Nasotracheal intubation in patients with basilar skull fractures should be exercised with extreme caution to avoid intracranial tube placement, since this complication has been documented extensively with nasogastric tube insertion(6-9).Rapid sequence induction with thiopentone or propofol and suxamethonium and intubation while maintaining cricoid pressure and manual inline axial stabilization is recommended. But if the airway is difficult, hypnotics and muscle relaxants are contraindicated unless the ability to ventilate with a bag and mask has been established. Administration of thiopentone or propofol in a hypovolemic patient may decrease the systemic arterial blood pressure and thereby the cerebral perfusion pressure (CPP). A profound decrease in CPP caused by these agents may be more detrimental to cerebral oxygenation than a transient increase in ICP due to intubation. Cerebral blood flow (CBF) in a patient with TBI is lowest during first 24 hrs after injury, which is the time when tracheal intubation is required. There is no consensus on the choice of anaesthetic agent for reduction of ICP during tracheal intubation in patients with TBI. Based on the evidence from studies on tracheal suctioning, prevention of cough by a muscle relaxant seems to be more effective in decreasing the ICP than administering other adjuvants such as thiopentone,fentanyl or lignocaine(10). Barbiturates and lignocaine were, however, effective in attenuating ICP increase caused by tracheal suctioning in patients who were received muscle relaxants. Choice of muscle relaxant also remains somewhat controversial. Suxamethonium causes a transient increase in ICP because of initial muscle fasciculation. Defasciculation with a small dose of non-depolarizing relaxant appears to prevent an increase in ICP. Hyperkalemic response to suxamethonium may be expected from 48 hrs onwards with peaks between 4 weeks and 5 months. Rocuronium also facilitate rapid intubation because of its rapid onset of muscle relaxation now considered to be the ideal agent.

Resuscitation of oxygenation and blood pressure

Early post-injury episodes of hypotension or hypoxia greatly increase morbidity and mortality from severe head injury. At present, defining level of hypotension and hypoxia is unclear in these patients. However, ample class II evidence exists regarding hypotension, defined as a single observation of a systolic blood pressure of <90mm Hg, or hypoxia, defined as apnea/cyanosis in the field or a PaO2 < 60 mm Hg by arterial blood gas analysis, considered to be detrimental and these values must be avoided, if possible, or rapidly corrected in severe head injury patients. A significant proportion of adult and pediatric TBI patients are discovered to be hypoxemic or hypotensive in the pre-hospital setting. Patients with severe head injury that are intubated in the pre-hospital setting appear to have better outcomes. Strong class II evidence suggests that raising the blood pressure in hypotensive, severe head injury patients improves outcome in proportion to the efficacy of the resuscitation. Secondary injury to the brain is largely a result of ischemia and the cascade initiated by ischemia. Therefore, hypoxia and hypotension must be managed aggressively.

BTF (Brain Trauma Foundation) Guidelines (11) recommends: Hypotension (SBP < 90 mmHg) or hypoxia (apnea, cyanosis or SaO_2 < 90% or PaO2 < 60mm Hg) must be avoided or corrected immediately in severe TBI patients.

Options:

The MAP should be maintained above 90 mmHg through the infusion of fluids throughout the patient's course to attempt to maintain CPP > 70 mmHg. Patients with GCS < 9 who are unable to maintain

their airway or who remain hypoxemic despite supplemental O2 required that their airway to be secured by endotracheal intubation.

Fluid resuscitation

In patients without head injury, the Cochrane review (a data base for evidence-based medicine) in a meta-analysis of 16 trials, found no clearly defined benefit of administration of colloid over crystalloid (12). Due to the increased expense of colloid, and the potential for inducing coagulopathy with commonly used types of colloid such as hetastarch, its routine use in the multiply injured patient with head injury cannot be recommended. With an intact blood brain barrier, movement of fluid into the brain is primarily determined by the osmotic pressure gradient; thus, under normal conditions, the use of isotonic or hypertonic crystalloid would decrease cerebral edema by maintaining normal or increased osmolarity and sodium levels. It is theoretically possible for some patients with a partially disrupted blood brain barrier to benefit from the use of colloid, as demonstrated by Drummond et al in experimental brain injury (13).A similar approach is used in the lund therapy (14).On balance, there is insufficient evidence to justify the use of colloid for patients with TBI.

Fluid resuscitation in initial stages should be carried out aggressively without undue concern for increasing brain edema. Withholding fluid resuscitation for fear of increasing brain edema is detrimental to the CBF and cerebral oxygenation. Hypotonic solutions should be strictly avoided during fluid resuscitation. Even large volumes of ringer's lactate should be avoided, as it is mildly hypo tonic. Care should be taken to see that plasma osmotic and oncotic pressures are not decreased by inappropriate fluid therapy. Glucose containing solutions should also be avoided since glucose levels >200 mg/dl have been associated with poor neurological outcome. It is not clear whether the poor outcome is a result of hyperglycemia acting as a marker of more severe head injury, or if the stress induced hyperglycemia, in the presence of ischemia, causes a lactic acidosis in the brain and worsens outcome. More over PET scan study has shown regional hyperglycosis in patients with severe TBI.

Indications for intracranial pressure monitoring

BTF Guidelines:

Comatose head injury patients (GCS 3-8) with abnormal CT scans should undergo ICP monitoring. Comatose patients with normal CT scans have a much lower incidence of intracranial hypertension unless they have two or more of the following features at admission: age over 40, unilateral or bilateral motor posturing, or a systolic blood pressure of less than 90 mm Hg. ICP monitoring in patients with a normal CT scan with two or more of these risk factors is suggested as a guideline.

Routine ICP monitoring is not indicated in patients with mild or moderate head injury. However, it may be undertaken in certain conscious patients with traumatic mass lesions at the discretion of the treating physician.

Intracranial pressure treatment threshold

Guidelines:

An absolute ICP threshold that is uniformly applicable is unlikely to exist. Current data, however, support 20-25 mm Hg as an upper threshold above which treatment to lower ICP should generally be initiated.

Options:

Interpretation and treatment of ICP based on any threshold should be corroborated by frequent clinical examination and CPP data.

Recommendations for intracranial pressure monitoring technology

In patients who require ICP monitoring, a ventricular catheter connected to an external strain gauge transducer or catheter tip pressure transducer device is the most accurate reliable method of monitoring ICP and enables therapeutic CSF drainage. Clinically significant infections or hemorrhage associated with ICP devices causing patient morbidity are rare and should not deter the decision to monitor ICP. Parenchymal catheter tip pressure transducer devices measure ICP similar to ventricular ICP pressure but have the potential for significant measurement differences and drift due to the inability to recalibrate. These devices are advantageous when ventricular ICP is not obtained or if there is obstruction in the fluid couple. Subarachnoid or subdural fluid coupled devices and epidural ICP devices are currently less accurate.

Guidelines for cerebral perfusion pressure

Option:

Maintenance of a CPP above 70 mm Hg is a therapeutic option that may be associated with a substantial reduction in mortality and improvement in quality of survival and is likely to enhance perfusion to ischemic regions of the brain following severe TBI. No study has demonstrated that the incidence of intracranial hypertension, morbidity, or mortality is increased by the active maintenance of CPP above 70 mm Hg by normalizing the intravascular volume or inducing systemic hypertension.

Hyperventilation

Adequate ventilation must be established in TBI patients because elevated PaCO2 levels cause cerebral vasodilation and increase in cerebral blood flow by approximately 3-4% per mm Hg PaCO2. This increase in CBF, although theoretically desirable, is associated with increase in CBV, which will further increase ICP, thereby reducing CPP. However, excessive hyperventilation (PaCO2 <30 mm Hg) to reduce ICP should be avoided since hypocarbia causes cerebral vasoconstriction and reduction in CBF and can worsen ischemia.

Standard:

In the absence of increased ICP chronic prolonged hyperventilation therapy ($PaCO_2 \leq 25$ mmHg) should be avoided after TBI.

Guidelines:

The use of prophylactic hyperventilation ($PaCO_2 \leq 30$ mmHg) during the first 24 hrs after severe TBI should be avoided because it can compromise cerebral perfusion during a time when the CBF is already reduced.

Options:

hyperventilation may be necessary for brief periods when there is acute neurological deterioration or for longer periods if there is refractory intracranial hypertension. SjO2, AJDO2, PtiO2 and CBF monitoring may help to identify cerebral ischemia if hyperventilation is necessary. Chronic prophylactic hyperventilation therapy should be avoided during the first 5 days after severe TBI and particularly during the first 24 hrs. CBF measurements in patients with severe TBI demonstrate that blood flow early after injury is low and strongly suggest that in the first few hours after injury the absolute values approach those consistent with ischemia. AVdO2 and SjO2 and brain tissue O2 measurements corroborate these findings. Hyperventilation will reduce CBF values even further, but will not consistently cause a reduction of ICP and may cause loss of autoregulation. The cerebral vascular response to hypocapnia is reduced in those with the most severe injuries (subdural hematomas and diffuse contusions), and there is substantial local variability in perfusion. While the CBF level at which irreversible ischemia occurs has not been clearly established, ischemic cell change has been demonstrated in 90% of those who die following TBI, and there is PET scan evidence that such damage is likely to occur when CBF drops below 15-20 ml/100 g/min. A prospective randomized clinical trial has determined that outcomes are worse when TBI patients are treated with chronic prophylactic hyperventilation therapy. Within the standard, guideline, and options, specific $paCO_2$ thresholds have been described that are different for each of the three parameters. These individual thresholds were selected based on the preponderance of literature supporting those thresholds in the contexts of the statements, which included them. With the exception of the threshold included for the standard in this guideline, it is emphasized that the $paCO_2$ threshold is not as important as the general concept of hyperventilation. The preponderance of the physiologic literature concludes that hyperventilation during the first few days following severe traumatic brain injury, whatever the threshold, is potentially deleterious in that it can promote cerebral ischemia.

Use of Mannitol

Guidelines:

Mannitol is effective for control of raised ICP after severe TBI. Effective doses range from 0.25 to 1 g/kg/body weight.

Options:

Indications to its use prior to ICP monitoring are signs of transtentorial herniation or neurological worsening not attributable to extracranial pathology. Hypovolemia should be avoided by adequate fluid replacement.Serum osmolarity should be kept below 300 mOsm because of concern for renal tubular toxicity and acute renal failure. A Foley catheter is essential in these patients. Some patients may require loop diuretics after mannitol to achieve a significant diuresis. Mannitol may initially cause an increase in central venous pressure and CBF, with a transient increase in ICP. Intermittent boluses may be more effective than continuous infusion.The evidence supporting use of mannitol for ICP control is sufficiently strong to warrant guideline status. Mannitol is effective in reducing ICP, and its use is recommended as a guideline in the management of traumatic intracranial hypertension. Serum osmolalities >320 mOsm and hypovolemia should be avoided. There is some data to suggest that bolus administration is preferable to continuous infusion. The duration of reduction in ICP is usually about 90-120 minutes, and a rebound increase in ICP may occur. In presence of hypovolemia, mannitol administration could be deleterious ("paradox effect") due to a further increase in renal salt and water excretion that could lead to a drop in MAP with a consequent drop in CPP that could start the so-called vasodilatadory cascade and increase ICP.

Hypertonic saline (HTS) in concentrations of 3%, 7.5%, 10% or 23.4% has been advocated by some groups for reducing ICP.HTS appears to provide a greater reduction in ICP for a longer duration than mannitol, and it does not exacerbate hypovolemia since it is not a diuretic.However, it can cause hypernatremia and often results in rebound hypertension.

Use of barbiturates in the control of intracranial hypertension

Guideline:

High-dose barbiturate therapy is efficacious in lowering ICP and decreasing mortality in the setting of uncontrollable ICP refractory to all other conventional medical and surgical ICP-lowering treatments, in salvageable TBI patients. Utilization of barbiturates for the prophylactic treatment of ICP is not indicated. The potential complications attendant on this form of therapy mandate that its use be limited to critical care providers and that appropriate systemic monitoring be undertaken to avoid or treat any hemodynamic instability. When barbiturate coma is utilized, consideration should also be given to monitoring arteriovenous oxygen saturation as some patients treated in this fashion may develop oligemic cerebral hypoxia.

The use of CVP or Swan Ganz catheters and arterial lines will be helpful in the hemodynamic management in these patients.

Role of steroids

Standard:

The majority of available evidence indicates that steroids do not improve outcome or lower ICP in severely head-injured patients. The routine use of steroids is not recommended for these purposes.

Nutrition

Guidelines:

Replace 140% of resting metabolism expenditure in nonparalyzed patients and 100% in paralyzed patients using enteral or parenteral formulas containing at least 15% of calories as protein by day 7 after injury.

Options:

The preferable option is use of jejunal feeding by gastrojejunostomy due to ease of use and avoidance of gastric intolerance.

Data show that starved head-injured patients lose sufficient nitrogen to reduce weight by 15% per week. Class II data show that

100-140% replacement of resting metabolism expenditure with 15-20% nitrogen calories reduces nitrogen loss. Data in non-head injured patients show that a 30% weight loss increases mortality rate. Class I data suggests that non-feeding of head-injured patients by the first week increases mortality rate. The data strongly support feeding at least by the end of the first week. It has not been established that any method of feeding is better than another or that early feeding prior to 7 days improves outcome. Based on the level of nitrogen wasting documented in head-injured patients and the nitrogen sparing effect of feeding, it is a guideline that full nutritional replacement be instituted by day 7. Nutritional support can be started as soon as the patient recovers the GI transit and if ICP and CPP are in the desired range without the use of vasoactive drugs.

Role of antiseizure prophylaxis following head injury

Standard:

Prophylactic use of phenytoin, carbamazepine, phenobarbital or valproate, is not recommended for preventing late posttraumatic seizures.

Options:

Anticonvulsivants may be used to prevent early PTS in patients at risk. This prevention does not indicate an improvement in outcome.

The majority of studies do not support the use of the prophylactic anticonvulsants for the prevention of late PTS. Routine seizure prophylaxis later than 1 week following head injury is, therefore, not recommended. If late PTS occur, patients should be managed in accordance with standard approaches to patients with new onset of seizures. Phenytoin and carbamazepine have been shown to reduce the incidence of early PTS. Valproate may also have a comparable effect to phenytoin on reducing early PTS but may also be associated with a higher mortality. It is, therefore, an option to use phenytoin or carbamazepine to prevent the occurrence of seizures in high-risk patients during the first week following head injury.

Surgical management of traumatic intracranial lesions

(The EBIC Guidelines for management of Severe Head Injury in adults) (15).

Traumatic intracranial lesions that require surgical intervention must be treated as quickly as possible to obtain the best neurological outcome. Delay in craniotomy of more than 3 hrs from the time patients exhibit bilaterally fixed and dilated pupils has been associated with a significant increase in morbidity and mortality (16). There were no

survivors when the craniotomy was delayed for more than 6 hrs. Intracranial compression must be relieved as quickly as possible to minimize the extent of secondary injury.

The EBIC guidelines do not differ too much from the BTF guidelines. They enrich them with the surgical treatment timing and indications that could be summarized as follows:

Acute epidural (extradural) hematomas

An extradural hematoma is defined as a collection of blood between the duramater and the skull. It is most commonly caused by laceration or tearing of the middle meningeal artery but can also be caused by venous bleeding. Delayed presentations can occcur in up to 30% of cases, which underscores the need for ICP monitoring and close monitoring of neurological status(17). Repeat CT scan should be performed at 12 to 24 hrs after injury to look for delayed lesions , as well as to evaluate the extent of cerebral swelling.One third of these patients exhibits a brief lucid interval followed by a decreased level of consciousness. The death rate from extradural hematoma is very low (5%), unless there is signifcant delay in diagnosis and treatment(17). There is usually little underlying bain injury, and these patients generally have a good neurological outcome unless evacuation delayed. Significant hematomas should be evacuated immediately upon detection.

Acute subdural hematoma (Contusions)

Acute subdural hematoma (SDH) is defined as a collection of blood between the dura mater and the brain. These traumatic lesions causes significant intracranial pathology than extradural hematoma. The neurological outcome from acute SDH , even when evacuated early is commonly poor. Underlying diffuse axonal injury is frequently present and the release of excitotoxic aminoacids from the dying cells may be responsible for the onset of delayed ischemia. For small hemorrhagic contusions or other small intracerebral lesion a conservative approach is generally adopted. But operation should be considered urgent for large intracerebral lesions with high or mixed density on CT scan.

Specific indications for operations include:

a Clinical deterioration

b) Size > 1cm thick extracerebral clot. Volume > 25 – 30 ml in intracerebral hematomas.

c) Midline shift > 5 mm.

d) Enlargement of contralateral ventricle (temporal horn).

e) Obliteration of basal cisterns or third ventricle.

f) Raised or increasing ICP

Skull Fractures

Depressed fractures are divided in to open and closed, depending on the presence of overlying scalp laceration or communication with an air sinus. Either type may cause underlying parenchymal damage or dural tear.In 5 -10% cases of depressed skull fractures is associated with an intracranial hemorrhage. Emergent surgical intervention is indicated to decrease the risk of infection by removing any foreign bodies and closing the dura and to restore normal surface anatomy. Operations definitely indicated only if it is a compound (open) fracture (not over sagittal sinus) or if the fracture is so extensive that it causes mass effect. Closed depressed skull fractures are usually treated conservatively, but operation may be appropriate in selected cases to reduce mass effect or correct defigurement.

Decompressive craniectomy

Decompressive craniectomy for patients with severe cerebral swelling refractory to maximal medical therapy as been found to be beneficial when patients are operated on early(within 24-48 hrs after injury) and before the ICP reaches 40 mm Hg (18,19). This procedure has been shown to reduce ICP and raise CPP, there by improving blood flow to areas of brain at risk of ischemia. The timing of this procedure is important to minimize secondary injury from ischemia. These patients are usually brought back months later for replacement of their bone flap or molding of an acrylic flap once the brain has reached full recovery.

Timing of surgery for other injuries

Timing of fracture repair in patients with TBI is controversial. The risk of delay in repair include worse functional outcome, with possible nonunion and longer hospital stay. The risk of increased pulmonary complications associated with fracture repair remains debatable since there are studies that support both early and delayed repair. With regard to the brain the concern for repairing fracture early (within first 24-48 hrs) is increased incidence of intraoperative hemodynamic instability with low CPP, and of intraoperative hypoxemia (SpO2 <90%) that occurs in many paients during the early phase after injury. Delaying surgery for non-life threatening injuries until the patient is more stable with respect to hemodynamics, pulmonary function,and ICP will provide the optimal conditions for the injured brain. However, if surgery cannot be delayed, CPP and oxygenation must be closely monitored to minimize the risk of cerebral ischemia.

TBI patients with subarachnoid hemorrhage may also suffer secondary ischemia from vasospasm. The onset of this vasospam is slightly earlier than that seen with aneurismal SAH. Depending upon the severity of head injury the incidence of vasospasm varies between

27% and 40%. GCS score on admission is inversely related to the development of vasospasm. Patients with severe vasospasm should have the nonemergent surgery delayed until the condition is resolved. The vasospam is characterized by increased blood flow velocity by transcranial Doppler sonography. Patients with mild to moderate vasospasm should be carefully evaluated before administering anaesthesia. MAP should be normal to elevated, and patients should be euvolemic to hypervolemic.Blood transfusion should be given for Hb less than 8 gm to optimize cerebral oxygen delivery. Standard treatment used for vasospam in aneurismal SAH such as "triple H therapy" (hypertension, hypervolemia, and hemodilution) is efficacious, although calcium channel blockers appear to be ineffective. Patients who are symptomatic despite standard therapy may respond to angioplasty of the vasospastic vessel or direct intra-arterial injection of papaverine.

Aneasthetic management includes

1. rapid assessment of the ABCs of resuscitation should be done
2. pulse oxymetry and capnography provide rapid assessment of oxygenation and ventilation.
3. PEEP should be used judiciously before opening the dura because high PEEP can elevate ICP
4. ICP monitoring will provide an idea of MAP required to maintain a CPP of above 70 mm Hg
5. use of adequate volume replacement with iso-osmolar or hyperosmolar fluids and /or vasopressor is recommended
6. blood gas analysis to evaluate pH,PaO2,PaCO2,lactate levels and electrolytes, glucose, hematocrit and coagulation parameters should be obtained and appropriate management should be undertaken.
7. Invasive arterial blood pressure monitoring is recommended because abrupt changes in BP can occur in multiply injured patients during dural opening in acute SDH
8. CVP monitoring is helpful in assessing the volume status. In the absence of CVP monitoring, an estimate of volume status can be assessed by examining the systolic pressure variation on the arterial pressure tracing with positive pressure ventilation.
9. Pulmonary artery catheterization may be indicated when there is associated left ventricular dysfunction or pulmonary artery hypertension.
10. Retrograde jugular bulb catheters can be helpful in assessing whether the global oxygen delivery is adequate for the metabolic demand. Normal jugular bulb saturation (Sjvo2) is 65%, and any value below 50% is considered critical and indicative of potential cerebral ischemia.

11. Newer monitors of regional oxygenation for injured brain can measure the brain tissue partial pressure of oxygen (PtiO2), CO2 tension, and pH or tissue PO2 which may helpful in preventing secondary injury than monitors of global perfusion.
12. During maintenance of anaesthesia ,volatile agents such as isoflurane of sevoflurane should be used with a dose less than 1 MAC to avoid cerebral vasodilation .
13. Use of neuromuscular blockade will prevent any coughing or straining on the endotracheal tube, which can elevate ICP
14. Narcotics such as fentanyl or sufentanyl should be used for supplemental analgesia.
15. The use of N2O in trauma setting is controversial due to the potential for increasing the volume of any air-filled spaces, such as pneumothorax. It causes increase in CMRO2 and CBF there by increasing ICP (20).
16. Decompression hypotension can occur, either from raising the bone flap in extradural hematoma or with opening of the dura in subdural hematoma and when the ICP is suddenly reduced. This hypotension could be catastrophic if the patient is hypovolemic. Therefore every effort should be made to ensure euvolemia before dural opening. Preoperative predictors of hypotension on dural opening include low GCS score, absence of mesencephalic cistern on CT scan and bilaterally dilated pupils.

Control of intraoperative intracranial hypertension

Interventions at three different components of brain can be undertaken

1. cerebrospinal fluid

   ventriculostomy

2. Brain bulk

   osmotic /loop diurectics

   hypertonic saline

   craniectomy

   partial temporal lobectomy

3. Cerebral blood volume

   hyperventilation (risk of cerebral ischemia)

Hypothermia (risk of coagulopathy, infection, benefit is controversial)

Pharmacologic (thiopentone,propofol-avoid hypotension)

Head elevation 15-30^{o} (avoid decrease in MAP)

Maximize venous outflow (head in neutral position, no neck compression)

Sedation and paralysis

Avoid volatile anaesthetics at > 1 MAC

Avoid hypertension

Avoid hypotension and hypoxemia

Avoid hyperthermia.

In patients with mild injury or those recovered from their initial insult, tracheal extubation may be possible but should be done only after careful assessment of the ability to protect the airway, maintain SPO2>90% and adequate ventilation. If extubation is planned, judicious use of narcotics is recommended.

References

1. Acosta J, Yang J, Winchell R, et al. Lethal injuries and time to death in a level 1 trauma center. J Am coll surg 1998;186:528-533
2. Teasedale G, Jennett B: Assessment of coma and impaired consciousness. A practical scale.Lancet 1974;2:81-84
3. Lannoo E,Van Rietvelde F, Colardyn F et al. Early predictors of mortality and morbidity after severe closed head injury. J Neurotrauma2000;17:403-414
4. Michael D, Guyot D, Darmody W. coincidence of head and cervical spine injury. J neurotrauma 1989;6:177-189
5. lida H,Tachibana S,Kitahara T,et al. Association of head trauma with cervical spine injury, spinal cord injury or both. J Trauma 1999;46:250-252
6. Bahr W,Stoll P.Nasal intubation in the presence of frontobasal fractures:a retrospective study.J Oral Maxillofac Surg 1992;50:445-447
7. Rosen c, Wolfe R,Chew S, et al.Blind nasal intubation in the presence of facial trauma.J Emerg Med 1997;15:141-145
8. Rhee K, Muntz C,Donald P,et al.Does nasotracheal intubation increase complications in patients with skull base fractures? Ann Emerg Med 1993;22:1145-1147
9. Ferreras J, Junquera L, Garcia-consuegra L. Intracranial placement of nasogastric tube after severe craniofacial trauma. Oral Surg Oral Med Oral pathol Oral Radiol Endo 2000;90:564-566
10. White PF,Schlobohm RM, Pitts LH, Lindauer JM. A randomized study of drugs for preventing increasing intracranial pressure during endotracheal suctioning. Anesthesiology 1982;57:242-244
11. Brain Trauma Foundation. The American Association of Neurological surgeons.The joint section of neurotrauma and critical care. Resuscitation of blood pressure and oxygenation. J Neurotrauma 2000;17:471-478

12. Bunn f,Roberts I,Tasker R,et al. hypertonic versus isotonic crystalloid for crystalloid for fluid resuscitation in critically ill patients (Cochrane review). Cochrane database syst rev2000;4:cd002045

13. Drummond J,Patel P,cole D,et al . the effect of reduction of colloid oncotic pressure, with and without reduction of osmolality, on posttraumatic cerebral edema. Anesthesiology1998;88:993-1002

14. Eker C,Asgeirsson B,Grande Pet al.Improved outcome after severe head injury with a new therapy based on principles for brain volume regulation and preserved microcirculation.Crit Care Med 1998;26:1881-1886

15. EBIC Guidelines for Management of Severe Head Injury in Adults. Acta Neurochir (Wien) 1997;139:286-294

16. sakas D,bullock m, Teasdale G. one year outcome following craniotomy for traumatic hematomain patients with fixed dilated pupils. J Neurosurg 1995;82:961-965

17. Poon W , rehman s, Poon c, et al. Traumatic extradura hematoma of delayed onset is not a rarity. Neurosurgery 1992;30:681-686

18. Taylor A, Butt W, Rosefeld J, et al. A randomized trial of very early decompressive craniectomy in children with traumatic brain injury and sustained intracranial hypertension. Childs Nerv Syst 2001;17:154-162.

19. Polin R, Shaffrey M, Bogaev C et al. Decompressive bifrontal craniectomy in the treatment of severe refractory posttraumatic cerebral edema. Neurosurgery 1997;41: 84-92

20. Lam AM, Mayberg TS, Eng CC,et al. Nitrous oxide -sevoflurane anesthesia causes more cerebral vasodilation thanan equipotent dose of isoflurane in humans.Anesth analg 1994;78:462-468

Flow chart. Shows evidence -based protocol for treatment of raised ICP in TBI.