

Cardiopulmonary Bypass for Management of Intracranial Aneurysms: Anaesthetic Considerations

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Although advances in neurosurgical techniques have improved the surgical treatment of intracranial aneurysms, giant aneurysm surgery continues to be a technically difficult task with high operative morbidity. It remains a major technical challenge both for the neurosurgeon, and the neuroanaesthesiologist. Recent advances in cardiac surgery have fueled interest in the technique of deep hypothermic circulatory arrest for the treatment of giant and complex intracranial aneurysms. In addition, various other therapeutic techniques have been developed over time. In particular, the endovascular approaches such as coiling techniques, detachable balloons, etc. have gained wider acceptance in recent times. However, they may not be suitable for giant aneurysms and conventional surgical approach is still practiced that carries high morbidity and mortality. Such aneurysms are located in the posterior circulation and are large or giant in size. This group of difficult aneurysms requires the use of cardiopulmonary bypass (CPB) technique with hypothermia.

Justification for Undertaking CPB

One of the basic requirements during aneurysm surgery is cessation of blood flow within giant aneurysms. Although total local circulatory arrest can often be achieved with temporary clips, this is not always safe or even possible in certain anatomical situations. These conditions are termed *complex intracranial aneurysms*. There are numerous factors that make a given intracranial aneurysm "complex." These factors include location, configuration, size and presence of intraluminal

thrombus and/or calcification. Additionally, intraoperative misadventures may convert a "straightforward" aneurysm into a "complex" aneurysm. Finally, failed prior surgical attempts or failed endovascular therapy may make an aneurysm "complex." The conditions that necessitate the use of CPB can be summarized as follows:

- Large (10-25 mm diameter) or giant (> 25mm diameter) aneurysms of the posterior circulation.
- Giant left carotid aneurysm
- Aneurysms of the basilar artery bifurcation
- Patient with two aneurysms
- Aneurysms with a large neck making collapse almost impossible by temporary clipping
- Aneurysms with complex arterial base
- Presence of a thrombus or atheroma
- Aneurysms with fusiform configuration
- Failed endovascular coiling

CPB provides a non-pulsatile, lax aneurysm with prolonged safe period for surgical intervention. The reduction in blood flow into an aneurysm converts a hard, pulsating mass into a soft collapsed sac, allowing easy manipulation and dissection of the aneurysm. This also helps in precise clip application. The induction of hypothermia provides cerebral protection and increases brain tolerance to cerebral ischaemia. In the presence of profound hypothermia, temporary clips can be utilized for longer periods, which might not be safe in normothermic or mildly hypothermic conditions.

Recent advances in the field of cardiac surgery techniques have renewed interest on the role of CPB and induced hypothermia in intracranial aneurysm surgery. It has made new alternatives available for the management of *complex intracranial aneurysms*. These include use of deep hypothermic circulatory arrest using closed or open chest CPB^{1,2}, closed chest extracorporeal circulation with profound

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hypothermia³ moderate hypothermia with extracorporeal circulatory assistance,⁴ and selective brain cooling.⁵ Also, use of port-access CPB⁶ and adenosine induced transient arrest with hypothermia⁷ have been reported.

One major development has been the shift from open chest CPB to the closed chest CPB technique for noncardiac surgical interventions. Newer developments are aimed at further reducing the complications. These are directed at reducing the dose of heparin, use of circulatory assistance with hypothermia in place of circulatory arrest, and use of pharmacological interventions for transient circulatory arrest.

Hypothermia causes a significant reduction in cerebral oxygen consumption and protects the brain during hypoxic insults. The period of circulatory arrest tolerated at normothermia is 4-5 minutes, and doubles for every 8°C fall in temperature. (Table 1)

Table 1. Relationship between body temperature (°C), change in cerebral metabolic rate and duration of circulatory arrest tolerated.⁸

Body temperature °C	Normal cerebral metabolic rate (%)	Period of tolerated circulatory arrest (minutes)
38	100	4-5
30	50	8-10
25	25	16-20
20	15	32-40
10	10	64-80

Various studies have been conducted to assess the efficacy of moderate hypothermia (without CPB) in intracranial aneurysm clipping.^{9,10} Recently, Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST) a multicentre, prospective, randomized, partially blinded trial in patients with subarachnoid haemorrhage demonstrated that the use of mild hypothermia (target temperature 33°C) in the intraoperative period has no beneficial effects on the outcome.¹¹ CPB with deep hypothermic circulatory arrest was first used for aneurysm surgery by Patterson in 1962,¹² and Drake in 1964.¹³ Due to high incidence of untoward effects, the

technique was abandoned. However, the technique has been revisited in last decade due to improvements and safer CPB techniques. Since closed chest (femoral-femoral bypass) hypothermic circulatory arrest is the most common technique used for complex aneurysms, this is taken as a model for discussion in this article.

Approach to the Patient

The use of hypothermic CPB for aneurysm surgery requires a team approach. It has to be a planned procedure with appropriate role identification and cooperation of the team members. For this technique to be successful, the cooperation of neurosurgeon, cardiovascular surgeon, anaesthesiologist (well versed with the needs of cardiac and neurosurgical procedures), perfusionist and nursing staff is essential.

Preoperative evaluation: Preoperative evaluation needs to be directed towards detection of coronary or valvular heart disease, intrinsic pulmonary pathology, hypertension, peripheral arterial or venous disease that might complicate peripheral cannulation, significant renal or hepatic dysfunction, oesophageal conditions that might preclude transoesophageal echocardiography (TOE), and coagulopathy. Thus, the preoperative work-up includes complete blood count, coagulation profile (prothrombin and partial thromboplastin time), liver function tests including liver enzymes, renal function tests (blood urea, creatinine), ECG, and plain x-ray chest. In particular, aortic valve function should be carefully evaluated with transthoracic echocardiography because central cannulation and left ventricular venting through a median sternotomy is required if the aortic valve is incompetent. In general, many of these patients have healthy cardiovascular system so that the management of CPB is relatively uncomplicated. Medical history is sought in detail. The patients might be on calcium antagonists following an aneurysm rupture.

Anaesthesia technique: Various invasive and non-invasive monitoring devices are connected prior to induction of anaesthesia. These include connecting an ECG, pulse oximeter probe and invasive blood pressure monitoring. An arterial line

is inserted under local anaesthesia and sedation with midazolam and narcotic (fentanyl). However, the dose of sedation must be titrated on a case-to-case basis depending upon the sensorium of the patient in the preoperative period. A pulmonary arterial (PA) catheter is inserted after local infiltration or soon after induction of anaesthesia.

Anaesthesia is induced with moderate dose of fentanyl (10-50 µg/kg) and supplemented with thiopentone. Tracheal intubation is facilitated using a non-depolarizing muscle relaxant (rocuronium hydrochloride or vecuronium bromide). The patient is then connected to the anaesthesia ventilator so as to maintain arterial carbon dioxide tension (PaCO₂) of 30-35 mm Hg. To minimize the risk of intraoperative air embolism, nitrous oxide is generally avoided. External defibrillation pads are fixed on the chest. A bladder catheter is inserted to assess the urine output. A nasopharyngeal temperature probe is positioned and fixed properly. (Some centres recommend simultaneous monitoring of tympanic membrane, rectal and axillary temperatures). At this stage a TOE probe should be inserted. On-line echocardiography is critically important when peripheral cannulation for CPB is considered. It helps to determine the ventricular volume and contractility (transgastric short axis mid- papillary view of the left ventricle). The position of the venous catheter at the cavo-atrial junction can be confirmed (bicaval view). TOE also helps in monitoring the right and left ventricular distension during bypass. When cardiac arrest is instituted, the competency of the aortic valve must be constantly assessed. Leaking through the aortic valve during cardiac standstill with peripheral pump circulation could lead to ventricular distension.

The patient is placed supine, and head fixed in the fixation ring with pins. Top up dose of thiopentone or supplementation with isoflurane inhalation may be required to prevent the haemodynamic response to pin application. The patient is positioned and prepared in a manner to ensure that both the chest and the groin are prepared and accessible. Scalp electrodes for EEG monitoring are placed to achieve EEG signals.

Mannitol (0.5 – 1 gm/kg) is infused soon after commencement of craniotomy to enable brain laxity. Direct measurement of brain temperature can also be established. Baseline activated coagulation time (ACT) is determined to guide heparinization while on bypass.

The neurosurgeon and his team can now proceed with surgery till they reach the stage of 'inspection' of the aneurysm and the surrounding vessels. The intraoperative findings along with the preoperative radiological findings finally make them decide whether a CPB is required to proceed. This dissection time could vary between 2-4 hours after craniotomy and before bypass. The cardiac surgeon and his team step in to proceed with the bypass, once the decision has been made. Since closed chest (femoral- femoral) bypass is the most frequently adopted technique for clipping of aneurysms, the same is described.

Cannulation for CPB: Before femoral vessel cannulation, adequate heparinization is essential. This forms a very important step and must not be forgotten. A dose of 300 units/kg body weight is administered through the central line. A repeat ACT is performed after 5 min. The generally accepted ACT for establishing safe CPB is considered to be > 400 seconds.

Femoral Vessel Cannulation: The femoral artery and femoral vein can be cannulated by a percutaneous technique or by an open surgical exposure. With the availability of percutaneous kits, they are usually preferred over open surgical technique. The venous cannula is advanced till the right atrium. The position can be confirmed by TOE. Once the position of the cannula has been confirmed, and secured in place, CPB is initiated. Just before commencement of CPB, thiopentone or propofol is titrated in small doses (50 – 100 mg) to achieve EEG burst suppression. A continuous infusion is then established to maintain the EEG pattern till the patient is on bypass and circulatory arrest. It is resumed on re-warming. Additional bolus doses of muscle relaxant, fentanyl and midazolam are administered through central line to counteract the dilution effect of CPB.

Onset of Hypothermia: Once adequate flows (2 – 2.5 L/min) with a mean arterial pressure (MAP) of 50 mm Hg are achieved, hypothermia is initiated by cooling the oxygenated blood through the extracorporeal heat exchanger. The rate of cooling is dependant on total bypass flow and is often slower in femoral-femoral bypass than open chest bypass. Fluid loading and phenylephrine infusion may be necessary to maintain bypass flow at 2.5 L/min with a MAP of 50 mm Hg. TOE monitoring should be continuously performed.

Cardiac Arrest and Asystole: When ventricular fibrillation sets in, potassium infusion (20-80 mEq) may be given through the right atrial port of the PA catheter for asystole. Esmolol infusion has also been recommended to lower the fibrillatory threshold on cooling.¹⁴

When the brain temperature reaches about 15°C, circulation is arrested, and blood drained through the venous cannula to achieve cerebral vasculature relaxation and aneurysm laxity. Very low flows (trickle flows of 10 ml/kg/min) have been advocated by some workers who believe that it improves operating conditions dramatically, and can be tolerated for much longer periods (several hours) than complete circulatory arrest.¹⁴

The neurosurgeon can now proceed with clipping of the aneurysm. Once the aneurysm has been clipped, CPB is gradually re-established, and blood flows increased to attain near normal pressures to assess the haemostasis and test the aneurysm repair. After confirming satisfactory clipping of the aneurysm, rewarming is commenced. The safe period of circulatory arrest is generally accepted to be 45 minutes at 15°C. However, shorter periods are usually required.

Termination of Bypass: It is important to ensure normal arterial blood gas, acid base and electrolyte status before terminating the CPB. Sodium nitroprusside infusion can be used to control the arterial vascular resistance and blood pressure. As rewarming proceeds, spontaneous cardiac rhythm re-appears. In case there is ventricular fibrillation, external cardioversion using 200 – 400 J is used to

restore the rhythm. After attaining normothermia and satisfactory cardiac rhythm, the pump flows are gradually reduced and the CPB is terminated. Inotropes are generally not required if the cardiovascular system is normal.

Once off bypass, the effect of heparin is reversed using protamine (0.75–1.0 mg/100 units of heparin). ACT is measured to confirm heparin reversal. ACT < 150 seconds or within 10% of baseline values is considered acceptable. Heparin is reversed before closure of craniotomy. The femoral cannulae are removed and the craniotomy is closed.

Postoperative Care: The patient is transferred to the intensive care unit with all cardiac monitoring, and elective ventilation is continued till adequate return of sensorium and muscle power.

A schematic representation of the management plan in a patient with complex intracranial aneurysms is shown in figure 1.

Some Other Modifications

Moderate Hypothermia with Extracorporeal Assistance: Total circulatory arrest may not be necessary in all cases. A successful clipping of the basilar artery aneurysm using moderate hypothermia (27–30°C), closed chest CPB using femoral-femoral bypass to assist rather than substitute spontaneous circulation has been reported by Yamada et al.⁴ These authors hypothesized that such a technique entailed fewer disadvantages than deep hypothermic circulatory arrest with regards to intraoperative risks and postoperative complications. The authors used PA catheter with pacing (to treat sinus bradycardia due to hypothermia) and external pads (upper right chest and back) for defibrillation / synchronized cardioversion. They also utilised a lower target ACT of 250 seconds. Propofol infusion titrated to achieve burst suppression of raw EEG was used for cerebral protection. The technique looks promising but further studies are necessary to validate these results.

Heparin Bonded Circuits: In an attempt to

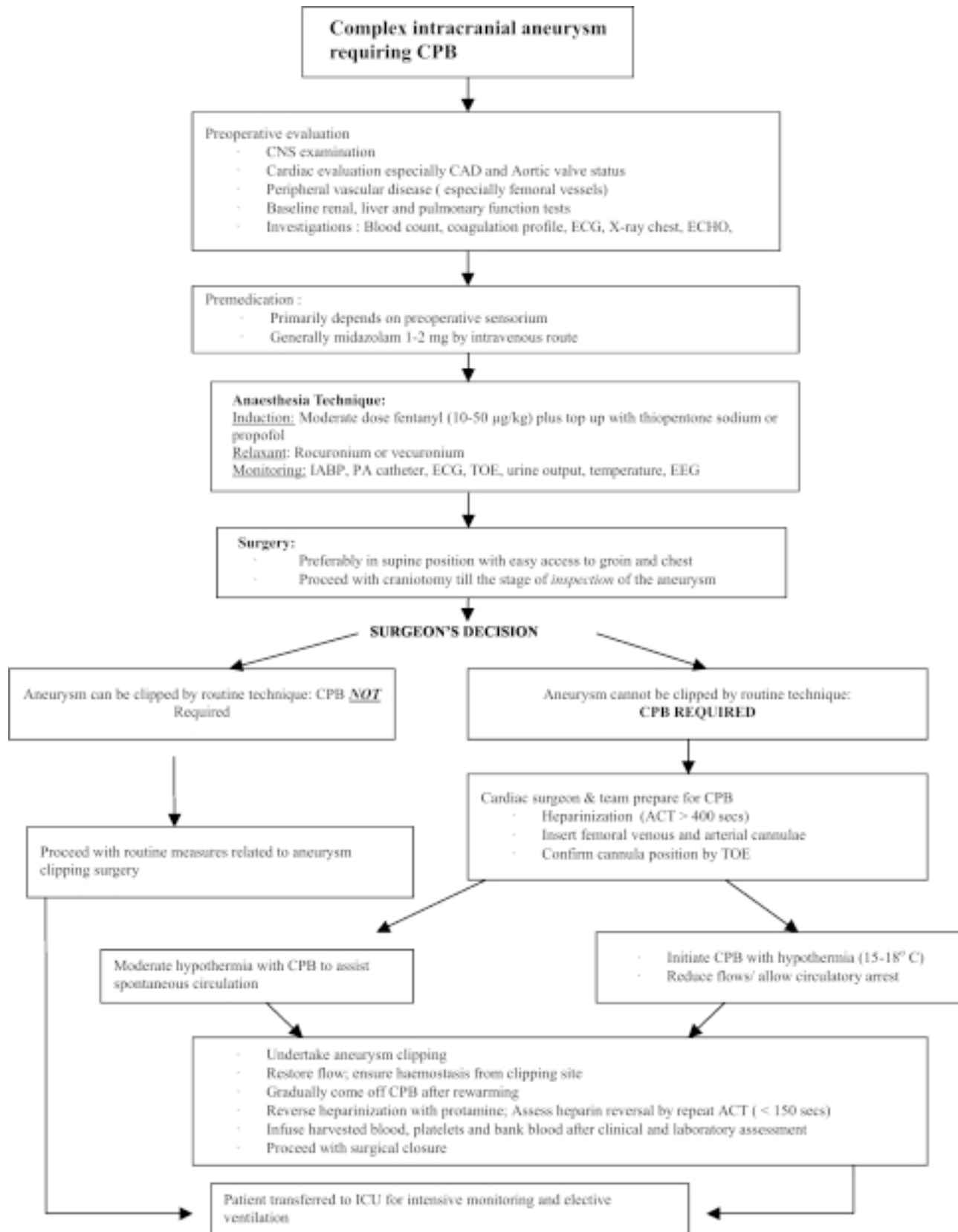


Fig. 1. Schematic representation of the management plan for clipping of complex intracranial aneurysm under closed chest hypothermic circulatory arrest. CAD: coronary artery disease, ECHO: echocardiography, IABP: intra-arterial blood pressure, TOE: trans-oesophageal echocardiography, ECG: electrocardiography, CPB: cardio pulmonary bypass, EEG: electroencephalogram, PA: pulmonary artery. ACT: activated clotting time

decrease the heparin requirement during CPB, heparin coated circuits have been developed. Heparin is bound ionically to plastic surfaces. This can decrease thrombus formation and platelet adhesion upon artificial surfaces. Many authors have used such circuits to institute femoral-femoral CPB in patients undergoing cerebral aneurysm surgery.¹⁵⁻¹⁸ Morishita et al¹⁶ have reported that the heparin requirement can be reduced to 1/3rd of the conventional dose.

Selective Brain Cooling: Extracorporeal femoral to carotid artery perfusion has been tried for selective brain cooling in a patient with giant aneurysm.⁵ While the brain temperature was 22°C

profound hypothermia, circulatory arrest and CPB. Further, heparin is not needed in this technique.

Subarachnoid Catheters: In an effort to have a lax brain, certain centres recommend the insertion of subarachnoid catheters to drain the cerebral spinal fluid. Since, the insertion of catheter is before heparinization, and the removal is after the effect of heparin has been reversed, the catheter related problems are unlikely. However, one must be vigilant for epidural or spinal haematoma in postoperative period.

Table 2 summarises some of the modifications that have been described.

Table 2. Summary of some modifications used in the management of intracranial aneurysms

Author (year)	No of cases	Body temperature	Duration of arrest	Remarks
Groff MW (1999) ⁷	1	32.5 °C	8 secs + 13 secs + clip application	Use of adenosine for transient asystole administered thrice.
Mesana T(2000) ¹⁷	8	15 – 18 C	20 ± 12 mins.	Use of centrifugal pumps and heparin-coated circuits.
Yu CL (2000) ¹⁹	1	Deep hypothermia		DHCA with retrograde cerebral perfusion.
Chen YS (2001) ¹⁵	4	Deep hypothermia	Mean ECMO time : 270 ± 105 min.	Heparin-bonded ECMO without the bridging tube and the cardiotomy reservoir.
Massad MG(2001) ¹	16	16 °C	Mean time 32 mins.	Closed chest CPB is safe and associated with less complications than conventional CPB.
Hachiro Y(2002) ¹⁸	8	20 °C		Heparin coated circuits and low dose heparin used.
Ohashi I (2003) ⁶	2	Not indicated		Port-Access EndoCPB system used.
Yamada M (2003) ⁴	1	27 – 30 °C	None	Extra corporeal circulatory assistance.
Lownie SP (2004) ⁵	1	Brain : 22°C Core : 35 °C	None	Selective brain cooling by extracorporeal femoral to carotid artery perfusion.

DHCA: deep hypothermic circulatory arrest, ECMO: extracorporeal membrane oxygenation, CPB: cardiopulmonary bypass

after 20 minutes of perfusion, the core temperature was above 35°C.

Adenosine: Adenosine (6 mg) has been used in conjunction with moderate hypothermia (32.5°C) to induce transient cardiac asystole to facilitate aneurysm clipping.⁷ The authors believe that the technique provides a near complete collapse of the aneurysm, and avoids complications secondary to

Cerebral Protection

This is one of the major concerns during clipping of the aneurysm. The exact mechanism is not known. Studies suggest that oxygen-centered free radicals cause brain injury associated with trauma and stroke. These reactive oxygen species may be detoxified by endogenous antioxidants, but cell death occurs

after antioxidants become depleted. Various intravenous and inhalational agents have been used for cerebral protection. General anaesthetics penetrate into brain parenchyma, where they may minimize oxidative injury to neurons by several mechanisms that prevent the initiation of free radical chain reactions or terminate the propagation of highly reactive radicals. First, general anaesthetics may inhibit free radical generation because these drugs slow cerebral utilization of oxygen and glucose, inhibit oxidative metabolism in neutrophils, and prevent reduction-oxidation changes in haemoglobin. Second, antioxidant anaesthetics, such as thiopental and propofol, directly scavenge reactive oxygen species and inhibit lipid peroxidation. Finally, anaesthetics may prevent the elevation of extracellular glutamate concentration and inhibit the activation of excitatory glutamatergic receptors that augment oxidative stress after ischaemia.

The burst suppression on EEG is taken as the end point to achieve cerebral protection during aneurysm surgery. Thiopentone, propofol and inhalational anaesthetic agents have been used to achieve cerebral protection. A survey on the current practice of pharmacological agents as cerebral protecting agents during deep hypothermic circulatory arrest revealed that 59% of respondents used thiopental, 29% used propofol and 48% used a variety of other agents, the most common of these being a steroid.²⁰

Thiopentone reduces the cerebral metabolic rate of oxygen (CMRO₂). Barbiturates may also have other actions like free radical scavenging and membrane stabilization. There is strong evidence to suggest that anoxic depolarization (AD) is an important factor in hypoxia/ ischaemia-induced neural damage. Treatments that prevent the occurrence of AD may be useful in providing neuronal protection against hypoxia. Recently published animal studies suggest that anoxic depolarization is prevented by thiopentone but not by propofol or isoflurane.²¹ Thiopentone in dose of 5-8 mg/kg results in 5 min of EEG suppression at normothermia. Proportional decreases in both cerebral blood flow (CBF) and CMRO₂ are produced. An infusion of 0.5 – 1.0 mg /kg/min is required for prolonged EEG suppression.

Monitoring EEG allows the anaesthesiologist to titrate the loading dose and maintenance infusion to achieve EEG burst suppression.

Propofol infusion in titrated doses to achieve EEG burst suppression has also been used for cerebral protection. Transient EEG burst suppression is obtained in dosages of 2-3 mg/kg and results in proportional decrease in CBF and CMRO₂. Infusion at the rate of 0.1-0.2 mg/kg/min produces EEG suppression and is rapidly metabolized.

Etomidate, like barbiturates, produces EEG burst suppression and reduces cerebral metabolic rate for glucose and oxygen. Clinically, etomidate decreases CBF, CMRO₂ and ICP whereas carbon dioxide (CO₂) reactivity, haemodynamic stability and cerebral perfusion pressure (CPP) are maintained.²² It inhibits release of excitatory neurotransmitters. It may be useful for neuroprotection when temporary vessel occlusion is required. It is routinely used in some centres to increase safety during temporary arterial occlusion employed for surgery of complex cerebral aneurysms. Doses of 0.4 to 0.5 mg/kg, cause burst suppression in less than 2 min in majority of patients. Consciousness is usually regained in 3 to 5 min due to redistribution. Additional doses in increments of 0.1 mg/kg may be given as electrical activity returns. Unlike thiopentone, it does not cause haemodynamic disturbances in the dose required to cause EEG burst suppression. However, the drug is known to cause adrenal suppression even after a single injection. EEG excitation and abnormal movements are other untoward effects of this drug.

Isoflurane in inspired concentrations of 2%-3% produces burst suppression. Unlike intravenous agents, burst suppression is not accomplished by decrease in CBF, although CMRO₂ is reduced. On comparison with propofol, Kanbak et al²³ reported that propofol offers no advantage over isoflurane anaesthesia for cerebral protection during CPB. However, they performed the study on patients undergoing coronary artery bypass grafting and whether these results can be extrapolated to aneurysm surgery is not known. Propofol has been reported to be a better agent for cerebral protection.²⁴

Myocardial Protection

This is achieved mainly by reduction in oxygen consumption by hypothermia, empty ventricle and asystole. Due to absence of the left ventricular vent, there may be over-distension of the left ventricle. This can be easily detected by TOE and if necessary, a left ventricular vent can be inserted by performing a small left thoracotomy or by converting to conventional open CPB procedure with sternotomy. Infusion of cardioplegia to provide myocardial protection is generally not available without aortic cross clamping, which necessitates sternotomy. However, the endo-aortic catheter (that has an inflatable balloon at the end of the catheter to act as aortic cross clamp) that are used in port-access surgery can be used, but reports in intracranial aneurysms are lacking. The right ventricular distension can be overcome by increasing the height of operation table. The use of centrifugal pumps in the bypass circuit also helps in venous drainage.

Acid Base Management

Whether to use pH-stat or alpha-stat management during deep hypothermic circulatory arrest is a controversial issue. In alpha-stat management, the temperature of blood is not corrected (taken as 37°C) and CO₂ is not added. While in pH-stat management, CO₂ is added to the oxygenator gas supply so that pH, if it was measured at the patient's hypothermic temperature would be maintained at 7.35 to 7.45. As CO₂ is added to the oxygenator in pH-stat management, it leads to increased cerebral blood flow and hence more uniform brain cooling. This increased blood flow, however, may increase the embolic load to the brain. The relevance of these findings to

neurosurgical applications of deep hypothermic circulatory arrest is still unclear.

Management of Bleeding Problems

Postoperative bleeding is one of the most common complications of CPB and hypothermia. Extensive surgical trauma, prolonged blood contact with the artificial surface of the CPB circuit, high doses of heparin, and hypothermia are all possible triggers of a coagulopathy leading to excessive bleeding. Platelet activation and dysfunction also occur and are caused mainly by heparin, hypothermia, and inadequate protamine administration. A better comprehension of the multifactorial mechanisms of activation of coagulation, inflammation, and fibrinolytic pathways during CPB may enable a more effective use of the technical and pharmaceutical options which are currently available. Some centres advocate blood harvesting prior to initiation of CPB, which is transfused in the post bypass period in an attempt to conserve platelets and coagulation factors. The use of heparin coated circuits and cell saver are also directed in reducing transfusion requirements after CPB.

Conclusions

Complex intracranial aneurysms continue to be a challenge for the neurosurgeons and the anaesthesiologists. CPB with hypothermia has been used successfully in management of these complex intracranial aneurysms. The advent of better CPB circuits, and cerebral protection measures have made the CPB procedure more safe. The technique shall, therefore, continue to be in vogue till an ideal endo-vascular alternative is available for managing these conditions without CPB.

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