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Adenosine -induced flow arrest in facilitating clipping of complex cerebral aneurysm surgeries: a case series

[1]Dr. Radhika.B, [2]Dr. Sharon Linnet.P, [3]Dr.Vijaya Gandipan.A, [4]Dr. Ramesh.V, [5]Dr. Aparna.A, [6]Dr. Shameem Sunkesula, [7]Dr. M.Madhusudhan, [8]Dr. P.Hemalatha, [9]Dr. N.Hemanth, [10]Dr. Aloka Samantaray, [11]Dr. Hanumantha Rao Mangu

[1, 2] Junior Resident-III, [3, 4, 5] Junior Resident-II, [6]Assistant professor, [7,8]Associate Professor, [9]Professor, [10]Professor and Head, [11]Senior Professor

Department of Anaesthesiology, Critical Care and Pain medicine Sri Venkateswara Institute of Medical Sciences Tirupati-517507

***Corresponding Author:**
Dr. Shameem Sunkesula
Assistant professor, Department of Anaesthesiology, Critical Care and Pain medicine
Sri Venkateswara Institute of Medical Sciences Tirupati-517507

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ABSTRACT

Intracranial aneurysm is a life threatening condition with high mortality rate. Complex intracranial aneurysms are giant aneurysms measuring larger than 25mm in difficult locations of brain and cranial base. Clipping cannot be applied in difficult locations due to limited view or is even entirely impossible. Several techniques can be used intra operatively to facilitate aneurysm exposure and clip ligation. These include temporary clip application to the proximal feeding vessel either by cardio-pulmonary bypass, endovascular balloon occlusion with suction & decompression, hypothermic flow arrest with cardiac standstill, adenosine induced flow arrest , each method has its own indications and complications. Temporary clipping is one of the methods in surgical management of intracranial aneurysms. Adenosine administration has been used to facilitate microsurgical clipping in complex cerebral aneurysms is a novel and relatively safe method. Adenosine's rapid onset and offset and predictable action make it a valuable tool in cerebrovascular surgery with apparently low neurologic and cardiopulmonary morbidity in the perioperative period. Here we present a series of four intracranial aneurysm clipping ligation with adenosine induced flow arrest managed perioperatively with successful outcome in a tertiary care hospital.

Keywords: Cerebral aneurysm; Aneurysm clipping; Adenosine; Flow arrest

INTRODUCTION

Intracranial aneurysm is a life threatening condition with high mortality rate. Complex intracranial aneurysms are giant aneurysms larger than 25mm in difficult locations of brain and cranial base.[1] Craniotomy and clip ligation of intracranial aneurysm remains a mainstay of definitive therapy to prevent morbidity and mortality. Temporary clipping cannot be applied to large or deep aneurysms in narrow corridors or near the skull base where temporary clip ligation can further obscure a limited view or is even entirely impossible. Several techniques can be used intra operatively to facilitate aneurysm exposure and clip ligation. These include temporary clip application to the proximal feeding vessel either by cardio-pulmonary bypass, endovascular balloon occlusion with suction & decompression, hypothermic flow arrest with cardiac standstill, adenosine induced flow arrest , with each method has

its own indications and complications[Table 1].Transient flow arrest caused by induced adenosine administration has been used to facilitate microsurgical clipping in complex cerebral aneurysms as a novel and relatively safe method .[2] Here, we describe our experience of four cases [Table 2] done in our institute during month of october 2019 to December 2019, where adenosine induced flow arrest was utilized to facilitate placing the clip in the neck of aneurysm without any intraoperative complication, which is new to our institutional practice since October 2019.

Table 1: **Fast facts of adenosine**

Ideal criteria for drug induced flow arrest in vascular surgery include the following

- ✓ Predictable effects (especially degree and duration of hypotension)
- ✓ Few pharmacological side effects
- ✓ Titratability
- ✓ Technical feasibility and simplicity
- ✓ Low risk for procedure-related complications.

Pharmacology:

1.Nucleoside analogue

- ✓ Binds to cardiac A1 receptors, which are membrane G-protein coupled receptors

This leads to multiple cardiac effects, including

-Depress sinoatrial (SA) node activity

-Slow atrioventricular (AV) nodal conduction

- Decreases atrial contractility and ventricular automaticity

- ✓ Its half-life is 0.6–20 s.
- ✓ Effect is seen 10–20s after bolus injection of adenosine.
- ✓ Adenosine is rapidly cleared from blood by uptake into erythrocytes and vascular endothelial cells.

Contraindications :

Absolute:

- ✓ Severe reactive airway disease

Relative:

- ✓ Cardiac conduction abnormalitie
- ✓ Allergy
- ✓ Dipyridamole, methylxanthines inhibit adenosine breakdown , uptake and can increase levels
- ✓ Calcified or fibrotic aneurysmal wall/dome

CASE REPORT:

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Table 2: Patient characteristics and perioperative events

Variables	Patient1		Patient 2		Patient 3		Patient 4	
Age:	53		47		60		44	
Sex:	Female		Female		Female		Female	
Comorbidities :	Nil		Nil		Systemic Hypertension		Systemic Hypertension	
Presenting complaints:	Headache Vomiting Neck pain		Headache Vomiting Loss of consciousness		Deviation of angle of mouth Headache Altered sensorium Generalized weakness		Chronic Headache Neck pain	
Diagnosis:	Basilar top aneurysm with SAH in interpeduncular cistern		Left ICA Aneursym with SAH in suprasellar cistern		SAH with ACOM Aneursym		Giant ACOM Aneursym B/L MCA aneurysm	
Intraoperative adverse events:	Nil		Nil		One episode of bradycardia		Nil	
Adenosine dosage:	6mg		6mg		6mg		6mg	
Duration of asystole:	13secs		10secs		12secs		11secs	
Duration of hypotension:	46secs		48secs		50secs		45secs	
Extubation:	After 24hrs		After 24hrs		After 24hrs		After 24hrs	
GCS :	Admission	Discharge	Admission	Discharge	Admission	Discharge	Admission	Discharge
	$E_4V_5M_6$	$E_4V_5M_6$	$E_4V_5M_6$	$E_4V_5M_6$	$E_3V_5M_6$	$E_4V_5M_6$	$E_4V_5M_6$	$E_4V_5M_6$

ACOM - Anterior Communicating artery, MCA - Middle Cerebral Artery, ICA- Internal Carotid Artery, SAH - Subarachnoid Haemorrhage, IV - intravenous, GCS – Glasgow Coma Scale.

After thorough preanesthetic check up and exclusion of contraindications for adenosine administration,patients were started on Tab Pantop 40 mg od and Tab Nimodipine 60 mg 4th hrly.Sedative premedication was avoided.Written informed consent was taken from responsible attendent.Thorough check of anesthesia work station, emergency drugs, defibrillator and availability of cross matched blood was done before shifting the patients to the operating room(OR). ECG, NIBP, SpO_2 $EtCO_2$ were connected to the patients once they were shifted into OR.Under local anesthesia a 16G iv cannula and arterial line secured in radial artery with 20 G jelco.

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Preoxygenation was done with 100% O_2 for 3 min. Anaesthesia induction was done with Inj.Fentanyl 2mcg/kg, Inj.Propofol 2mg/kg or Inj. Thiopentone sodium 4mg/kg and Inj.Vecuronium 0.1mg/kg and tracheal intubation was performed using appppropriate sized ET tube. To blunt the hemodynamic response to laryngoscopy and intubation Inj .Xylocard 1.5mg/kg was given intravenously 90 sec prior. Patients were connected to anaesthesia ventilator circuit with respiratory rate 12-14/min, tidal volume 6-7 ml/kg and isoflurane titrated to 1-1.5%. Right subclavian vein was catheterized with 7Fr, 15cm triple lumen catheter for drug, fluid, dye and adenosine administration. Scalp block was given with Inj Bupivacaine 0.25 %. Patients were positioned with proper padding of pressure points while taking care to avoid undue neck flexion and lateral rotation.Inj fentanyl 1mcg/kg was supplemented during head pin insertion and periosteal elevation. Intraoperatively maintenance of anesthesia was done with isoflurane (1-1.5%), propofol infusion(20-50mg/hr) and vecuronium infusion(0.8mcg/kg/min). Inj Adenosine was administered once surgeon explored the aneurysm site and ready with the clip. 6mg of adenosine bolus was administered through the central line, flushed with 20 ml of normal saline which resulted in 10-15 sec of asystole and drop of 30-35 mmHg in systolic BP. Heart rate and rhythm spontaneously recovered in all patients except in patient 3, who required atropine administration 0.6 mg iv for bradycardia. After clip application,BP was maintained 20% above the baseline and CVP above 12 mm Hg with fluid administration and ionotrope infusion. Patients were shifted to post anaesthesia care unit (PACU) and ventilated electively till patients met extubation criteria. All the patients were extubated within 24 hours postoperatively after confirmation of successful clip placement using CT scan.Patients were discharged in haemodynamically stable condition.

DISCUSSION:

The management of intracranial aneurysm starts from the time of diagnosis with adequate optimisation of vitals especially blood pressure. Tab:Nimodipine was started preoperatively to counteract the narrowing of blood vessels after sub-arachnoid hemorrhage and to protect the brain against periods of ischemia.[3] Sedative premedication was avoided to prevent hypercarbia which in turn leads to cerebral vasodilatation, increased cerebral blood flow and intracranial pressure. During induction of anaesthesia and tracheal intubation, it is critical to avoid hypertension(20-25% above baseline) and increase in MAP to avoid the risk of rupture of aneurysm. Rupture of aneurysm during induction of anaesthesia is rare (2%),but mortality is very high (approximately 75%).[4] Laryngoscopy, tracheal intubation, head pin insertion, skin incision, periosteal elevation and dura matter incision are highly stimulating interventions. The resultant haemodynamic stimulation can cause a dangerous increase in the TMPG(Trans Mural Pressure Gradient) which is the difference of Mean Arterial Pressure(MAP) and IntraCranial Pressure (ICP)[Figure1]. Increase in the MAP or an abrupt decrease in ICP leads to an increase in the transmural pressure and risk of aneurysm rupture. [5].Blunting of such hemodynamic responses can be done with Inj Fentanyl 1mcg/kg or Inj Esmolol 0.5mg/kg or Inj Xylocard 1.5 -2mg/kg or by increasing the depth of anesthesia using inhalational anesthetics or boluses of Inj propofol 20 to 30 mg IV. Also care should be taken to preserve Cerebral Perfusion Pressure (CPP) which also is the difference between MAP and ICP. Inadvertent fall in CPP leads to cerebral ischemia. Maintaining a fine balance between TMPG and CPP is of utmost importance in aneurysm surgery.

A triple lumen catheter was secured in subclavian vein to prevent hinderance to cerebral venous return, for maintenance of higher CVP after clamp application, to counteract major fluid shifts, to administer vasopressors if required, to administer mannitol and for venous access if at all prolonged stay in PACU is required. $EtCO_2$ is maintained between 26-30 mmHg. Hypercarbia leads to vasodilatation and raised ICP whereas hypocarbia leads to vasoconsriction and impaired flow through collaterals during clip application predisposing to cerebral ischemia.Avoid excessive neck flexion and lateral rotation as it obstructs venous drainage and inturn leading to raise in ICP. Intraoperatively the goals of anaesthesia were to provide a relaxed brain that will allow minimal retraction pressure and to preserve CPP. Brain relaxation was ensured with 15-30 degree head end elevation, avoiding lateral rotation of neck, mannitol administration(0.5-2g/kg and Inj.Frusemide (0.25-1mg/kg) iv.

There are no specific guidelines for optimal bolus dose administration of adenosine.[6] In 1999, Groff

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et al reported the first use of adenosine bolus to clip an un-ruptured basilar tip aneurysm in one patient with concomitant infusion of sodium NP and gave three doses of adenosine: 6mg, then 12mg and then another 12mg, which caused 8–13s of profound hypotension (MAP ~15mm Hg) and allowed the safe and successful placement of a clip.[7] In 2010, Powers et al used adenosine by administering escalating doses of adenosine until 30s of asystole was achieved (6mg, 12mg, 18mg, 24mg and 36mg). They found a rate of 1mg adenosine resulting in 1s of asystole on average.[8].

After a thorough literature review, we have decided to start with initial dose of 6mg bolus followed by 12mg IV as per surgeons requirement depending upon the complexity of the surgery, the need for asystole duration requirement. Our experience suggest adenosine induced asystole to facilitate aneurysm clipping is a low risk procedure and can be adopted where temporary occlusion with clips is impractical, unsafe, or difficult. Further studies are warranted to further refine our understanding of the utility of adenosine during intracranial aneurysm surgery.

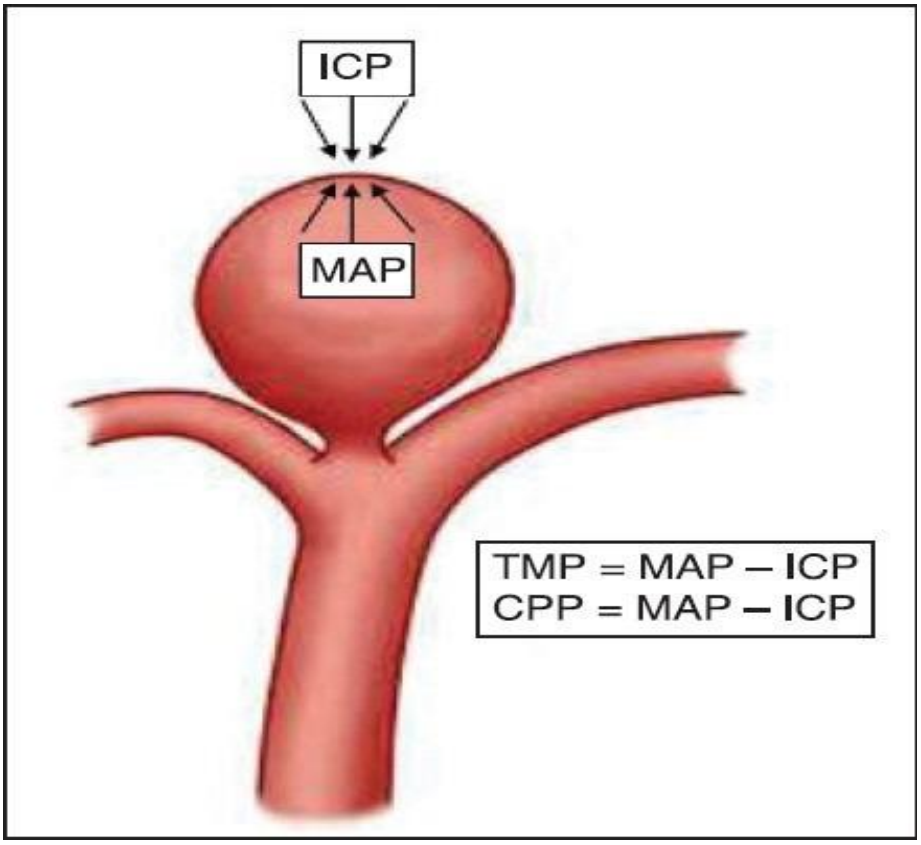

Figure 1:

CONCLUSION:

Adenosine- assisted flow arrest used for ruptured and unruptured aneurysms in anterior and posterior circulations with a rare incidence of clinically significant side effects. Its rapid onset and offset and predictable action make it a valuable tool in cerebrovascular surgery with apparently low neurologic and cardiopulmonary morbidity in the perioperative period.

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