CLINICAL Efficacy of dexmedetomidine in patients of moyamoya disease undergoing EDAS procedure - A retrospective analysis from Indian tertiary institute

Veena Ganeriwal1, Priyanka Agrawal2, Paulomi Dey3

1Associate Professor, Department of Anaesthesia, Grant Government Medical College, Mumbai, Maharashtra, India.
2Assistant Professor, Department of Anaesthesia, Grant Government Medical College, Mumbai, Maharashtra, India.
3Assistant Professor, Department of Anaesthesia, Grant Government Medical College, Mumbai, Maharashtra, India.

ABSTRACT

BACKGROUND
Moyamoya disease is a rare progressive, occlusive cerebrovascular disorder characterised by stenosis of the internal carotid arteries. The goal of surgical intervention in Moyamoya disease is to establish collateral blood flow with the intention of revascularising previously ischaemic areas of the brain. The most common procedure being Endovascular Angiogram Surgery (EDAS). Anaesthetic management of patients with Moyamoya Disease (MMD) focuses on maintenance of adequate cerebral blood flow, normalisation of intracranial pressure and avoidance of both cerebral vasoconstriction and vasodilatation. Dexmedetomidine is a short-acting alpha-2-adrenoceptor agonist which decreases mean arterial pressure, heart rate and has reasonable analgesic effect.

The objective was to study the effect of Dexmedetomidine as an anaesthetic adjuvant in Moyamoya disease patients.

MATERIALS AND METHODS
The study design is a retrospective descriptive study of 10 cases of Moyamoya disease, who underwent EDAS procedure at our tertiary care hospital between February 2015 and October 2017.

RESULTS
In all the 10 patients, intraoperative haemodynamic parameters and complications were noted. The mean heart rate and blood pressure in all the patients remained within 15% of baseline and steady during the study period, i.e. intraoperatively and 20 minutes postoperatively.

CONCLUSION
The effect of dexmedetomidine on the haemodynamic and recovery profile of these patients was found to be beneficial.

KEY WORDS
Moyamoya disease, Dexmedetomidine, EDAS Procedure.

useful in blunting haemodynamic responses in perioperative period due to its central sympatholytic effect. It has also shown neuroprotective effects in various experimental animals. Although, the exact mechanism remains unknown, dexmedetomidine is found to have antioxidan and anti-inflammatory properties, suppresses glutamate release and regulates apoptosis. It also preserves the regional CBF and produces an optimal balance in the microregional oxygen supply and consumption and improves oxygen balance during reperfusion.[12] Bradycardia and hypotension are the major side effects observed following dexmedetomidine infusion due to decrease in central sympathetic outflow. Hypotension is attributed to decreased central sympathetic outflow.[13]

**Aims and Objectives**
The aim of this study is to analyse and share our experience of conducting a series of 10 patients of Moyamoya disease under general anaesthesia and the effect of dexmedetomidine on their haemodynamic stability and recovery profile, which underwent EDAS procedure at our tertiary care institute.

**MATERIALS AND METHODS**
The study design is a retrospective descriptive study of Moyamoya disease conducted between February 2015 and October 2017 at tertiary care institute in India. All patients of Moyamoya disease diagnosed on Digital Subtraction Angiography who underwent EDAS procedure and aged between 5 and 50 years were included in this study.

Method adopted for administering anaesthesia in all cases were noted. It included standard monitoring like electrocardiography, pulse oximetry and end-tidal carbon dioxide monitor and invasive blood pressure for haemodynamic monitoring in place, all patients were premedicated with Inj. Glycopyrrolate 8 mcg/kg. Before induction, patients were given loading dose of dexmedetomidine (1 mcg/kg) over 10 mins. Induction of Anaesthesia was achieved with Inj. Fentanyl 2 mcg/kg, Inj. Propofol titrated to loss of eye lash reflex or number counting and Inj. Vecuronium 0.1 mg/kg. After endotracheal intubation intraoperative depth of anaesthesia was maintained with MAC of 0.8 of sevoflurane in 50% O2: Air. The patient’s ventilation was controlled to maintain normocapnic of EtCO2 between 28 - 32 mmHg. The patients also received continuous infusion of dexametomidine at the rate of 0.3mcg/kg/hr during intraoperative period. Haemodynamic parameters were noted intraoperatively and postoperatively till 20 minutes after extubation. In the postoperative period, patients were evaluated for analgesic requirements by visual analogue scale in initial 6 hrs. (Figure 2).

**RESULTS**
The patient’s clinical details are elaborated in Table 1. In patients of less than 12 years age, three presented with Transient Ischaemic Attack (TIA), while two patients presented with seizures. In adult patients, three presented with neurological deficit and two with altered sensorium. The mean heart rate and average Mean Arterial Pressure (MAP) in the study group are summarised in Table 2. The mean heart rate and blood pressure in all the patients remained within 15% of baseline and steady during the study period, i.e. intraoperatively and 20 minutes postoperatively. The postoperative pain in all patients was assessed with 10-point visual analogue scale and was found to be mild and tolerable. Immediate postoperative neurological and ischaemic complications were also less.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (Years)</th>
<th>Gender</th>
<th>Clinical Presentation</th>
<th>Diagnosis</th>
<th>Mean Heart Rate (+SD)</th>
<th>Mean Blood Arterial Pressure (SD)</th>
<th>Post-Operative VAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>F</td>
<td>Transient ischaemic attack</td>
<td>Bilateral internal carotid artery occlusion</td>
<td>88.6 (+8.5)</td>
<td>75 (8.4)</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>34</td>
<td>F</td>
<td>Right hemiplegia</td>
<td>Left parietal intraparenchymal haemorrhage</td>
<td>73.6 (9.2)</td>
<td>82 (12.6)</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>M</td>
<td>Left hemiplegia</td>
<td>Ischaemic infarct in right frontoparietal region</td>
<td>80.4 (7.2)</td>
<td>79.8 (9.5)</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>44</td>
<td>M</td>
<td>Altered sensorium, projectile vomiting</td>
<td>Left gangliocapsular intraparenchymal haemorrhage</td>
<td>75.9 (8.0)</td>
<td>80.9 (11.2)</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>F</td>
<td>Seizure</td>
<td>Suprachiasmatic ICA occlusion</td>
<td>95.3 (7.8)</td>
<td>72 (7.9)</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>M</td>
<td>Transient ischaemic attack</td>
<td>Infarct in right MCA territory</td>
<td>85.7 (9.1)</td>
<td>76.2 (6.9)</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>23</td>
<td>F</td>
<td>Altered sensorium</td>
<td>Bilateral ICA occlusion with intraparenchymal haemorrhage</td>
<td>93.2 (6.9)</td>
<td>82 (11.4)</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>7</td>
<td>M</td>
<td>Transient ischaemic attack</td>
<td>Periventricular ischaemic changes</td>
<td>75.8 (7.0)</td>
<td>88.3 (12.7)</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>4</td>
<td>F</td>
<td>Seizure</td>
<td>Periventricular ischaemic changes</td>
<td>77.9 (7.1)</td>
<td>74.5 (10.8)</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>16</td>
<td>F</td>
<td>Left hemiplegia</td>
<td>Ischaemic infarct in right parietal region</td>
<td>69.0 (7.2)</td>
<td>76.5 (7.3)</td>
<td>2</td>
</tr>
</tbody>
</table>

*Table 1. Patient Details*

**Table 2. Clinical Presentation, Diagnosis and Haemodynamic Parameters**
read to cerebral vasoconstriction, reduction of blood flow, control of inflammation and management of neurologic sequelae. Whereas, hypercapnia resulting from hypoventilation may lead to cerebral vasoconstriction, reduction of cerebral blood flow and precipitation of ischaemic symptoms. Whereas, hypercapnia resulting from hypoventilation which dilates normal cerebral vessels, generates minimal response from the diseased vessels in MM disease is to maintain a balance between oxygen demand and supply in the already compromised cerebral vasculature. Oxygen demand, i.e. increase in cerebral oxygen consumption is minimised by maintaining appropriate depth of anaesthesia and adequate analgesia, prevention of pressor response specifically during laryngoscopy, tracheal intubation, scalp pin application, surgical stimulus, while the supply is maintained by avoiding hypotension, maintaining normocarbia and adequate haematocrit. A decreased haematocrit due to anaemia or perioperative blood loss may compromise cerebral perfusion in MMD patients, hence a haematocrit of 30 - 42% is proposed to be adequate.

In children it is important to prevent perioperative crying, as it causes hyperventilation leading to hypocapnia with possible risk of cerebral vasocostriction, decreased cerebral blood flow and cerebral ischaemia. Effective premedication, smooth inhalational or IV induction and postoperative analgesia is imperative in preventing crying. Oral sedation for premedication should be adequate enough with care to avoid excessive sedation, which can cause hypotension and hypercapnia, another risk factor for cerebral ischaemia. Hypotension, if it occurs should be treated promptly with fluid and vasoconstrictors. During general anaesthesia, hyperventilation and resultant hypocapnia may lead to cerebral vasoconstriction, reduction of cerebral blood flow and precipitation of ischaemic symptoms. Whereas, hypercapnia resulting from hypoventilation which dilates normal cerebral vessels, generates minimal response from the diseased vessels in MMD which are already maximally dilated resulting in reduced blood flow to the area supplied. Hence, it is important to maintain normocapnia intraoperatively.

Perioperative blood pressure should be maintained at or above the pre-operative baseline. Hypotension should be avoided, which can reduce cerebral perfusion pressure in already compromised diseased vessels. Reduction in CBF is better tolerated in adults than children who have higher CMRO2 and hence are more prone to develop cerebral ischaemia due to hypotension.

Inadequate pain relief in postoperative period can lead to postoperative cerebral infarction. Multimodal strategy for postoperative analgesia including scalp block, opioid and non-opioid IV analgesics, per rectal paracetamol suppositories in children can provide adequate pain relief, calm awakening and reduced postoperative morbidity.

Maintaining cerebral perfusion perioperatively remains the goal. A variety of methods can help to estimate the adequacy of cerebral blood flow including end-tidal carbon dioxide monitoring and transcranial Doppler ultrasound which provides a non-invasive, objective and rapid method to assess cerebral blood flow and can be used to guide anaesthetic management. Transcranial Doppler can be used to assess cerebral blood flow during surgery and can help in adjusting the anaesthetic agents to maintain adequate cerebral blood flow. The goal for anaesthetic management in Moyamoya disease is to maintain a balance between oxygen demand and supply in the already compromised cerebral vasculature. Oxygen demand, i.e. increase in cerebral oxygen consumption is minimised by maintaining appropriate depth of anaesthesia and adequate analgesia, prevention of pressor response specifically during laryngoscopy, tracheal intubation, scalp pin application, surgical stimulus, while the supply is maintained by avoiding hypotension, maintaining normocarbia and adequate haematocrit. A decreased haematocrit due to anaemia or perioperative blood loss may compromise cerebral perfusion in MMD patients, hence a haematocrit of 30 - 42% is proposed to be adequate.

In children it is important to prevent perioperative crying, as it causes hyperventilation leading to hypocapnia with possible risk of cerebral vasocostriction, decreased cerebral blood flow and cerebral ischaemia. Effective premedication, smooth inhalational or IV induction and postoperative analgesia is imperative in preventing crying. Oral sedation for premedication should be adequate enough with care to avoid excessive sedation, which can cause hypotension and hypercapnia, another risk factor for cerebral ischaemia. Hypotension, if it occurs should be treated promptly with fluid and vasoconstrictors. During general anaesthesia, hyperventilation and resultant hypocapnia may lead to cerebral vasoconstriction, reduction of cerebral blood flow and precipitation of ischaemic symptoms. Whereas, hypercapnia resulting from hypoventilation which dilates normal cerebral vessels, generates minimal response from the diseased vessels in MMD which are already maximally dilated resulting in reduced blood flow to the area supplied. Hence, it is important to maintain normocapnia intraoperatively.

Perioperative blood pressure should be maintained at or above the pre-operative baseline. Hypotension should be avoided, which can reduce cerebral perfusion pressure in already compromised diseased vessels. Reduction in CBF is better tolerated in adults than children who have higher CMRO2 and hence are more prone to develop cerebral ischaemia due to hypotension.

Inadequate pain relief in postoperative period can lead to postoperative cerebral infarction. Multimodal strategy for postoperative analgesia including scalp block, opioid and non-opioid IV analgesics, per rectal paracetamol suppositories in children can provide adequate pain relief, calm awakening and reduced postoperative morbidity.

Maintaining cerebral perfusion perioperatively remains the goal. A variety of methods can help to estimate the adequacy of cerebral blood flow including end-tidal carbon
Dioxide (ETCO₂), invasive blood pressure monitoring and EEG. In our study, mean arterial pressure and ETCO₂ were used to measure CBF and cerebral perfusion considering intact autoregulation. A thorough preoperative neurological assessment and documentation of the neurological deficits should be done. Anaesthetic considerations include measures to optimise cerebral blood flow and minimise the risk of ischaemic and hyperaemic injury. Intraoperative goals include maintenance of stable haemodynamics, oxygenation and normocarbia (PaCO₂: 35 – 40 mmHg).\cite{25,26}

Dexmedetomidine, an imidazoline compound is believed to preserve the regional CBF and produce an optimal balance in the micro-regional oxygen supply and consumption. It also improves the oxygen balance during reperfusion and attenuates intraoperative haemodynamic responses. Dexmedetomidine has neuroprotective effects in various experimental studies done in animals. It can be used as an effective anaesthetic adjuvant for intraoperative haemodynamic stability and smooth emergence in patients with Moyamoya disease.\cite{27} undergoing revascularisation procedures. Also, it can provide brain protection effect by decreasing the level of excitatory amino acids. A meta-analysis conducted by Schnabel et al.\cite{28} revealed a lower risk for postoperative pain and the need for postoperative opioids following intraoperative dexmedetomidine in comparison with placebo or opioids in children undergoing surgery.

Cerebral hyperperfusion syndrome is characterised by focal neurological deficits due to cerebral oedema is a major postoperative complication after direct revascularisation surgery in Moyamoya disease. It presents as unilateral headache, facial pain, seizures and intracranial haemorrhage. Increase in cerebral blood flow following revascularisation, without reactive cerebral vasoconstriction, can lead to vasogenic cerebral oedema in Moyamoya disease due to impaired cerebral autoregulation and blood brain barrier. Treatment strategies include strict blood pressure control and administration of free oxygen radical scavengers. Dexmedetomidine has shown biochemical properties such as antioxidant effects, anti-inflammatory effects, suppression of glutamate release and apoptosis regulation, mechanism of which remains unknown. A study conducted by Seo H et al.\cite{29} showed that the duration of Cerebral Hyperperfusion Syndrome and length of hospital stay were shorter in patients who received intraoperative dexmedetomidine.

CONCLUSION
Moyamoya possesses lot of challenges to anaesthesiologist in terms of maintaining perioperative haemodynamic stability and smooth emergences from anaesthesia to avoid postoperative complications. Dexmedetomidine is known for having neuroprotective effect, as it helps to maintain haemodynamic stability, hence we tried to analyse the same effect in patients with Moyamoya disease. As the study was limited to very small number of patients, because of its fewer incidences in Indian population and further very few cases reporting to our institute, we can say that Dexmedetomidine can be useful as adjuvant for intraoperative haemodynamic stability.

REFERENCES


