A COMPARISON OF THE EFFECT OF ANAESTHESIA WITH SEVOFLURANE AND PROPOFOL ON CEREBRAL OXYGENATION DURING HYPERVENTILATION IN PATIENTS UNDERGOING SUPRATENTORIAL TUMOUR EXCISION – A RANDOMISED CONTROLLED STUDY

Dissertation submitted for the partial fulfilment for the

Requirement of The degree of DM Neuroanesthesia

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FEBRUARY 2022

DECLARATION

I hereby declare that this thesis titled "**A Comparison Of The Effect Of Anaesthesia With Sevoflurane and Propofol On Cerebral Oxygenation During Hyperventilation In Patients Undergoing Supratentorial Tumour Excision – A Randomised Controlled Study**" has been prepared by me under the capable supervision and guidance of Dr. Smita V, Additional professor, Division of Neuroanaesthesia and Neurocritical Care, Department of Anaesthesiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

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ABBREVIATIONS

ABG : Arterial blood gas

ASA : American Society of Anaesthesiologists

BIS : Bispectral Index

CBF : Cerebral blood flow

CBV : Cerebral blood volume

CMR : Cerebral metabolic rate

COPD : Chronic Obstructive Pulmonary Disease

CPP : Cerebral Perfusion Pressure

CSF : Cerebro spinal fluid

CTRI : Clinical Trial Registry-India

CVR : Cerebrovascular reactivity

DCS : Diffuse correlation spectroscopy

ECG : Electrocardiography

EEG : Electroencephalogram

$EtCO_2$ End tidal carbon dioxide

FiO_2 : Fractional inspired concentration of oxygen

GCS : Glasgow Coma Scale

HbO : Oxyhaemoglobin

ICP : Intracranial Pressure

IEC : Institutional Ethics Committee

MAC : Minimum alveolar concentration

MAP : Mean arterial pressure

NIRS : Near Infrared Spectroscopy

O_2ER : Oxygen Extraction Ratio

$PaCO_2$: Partial pressure of carbon dioxide in arterial blood

PaO_2 : Partial pressure of oxygen in arterial blood

$PbtO_2$: Brain tissue oxygen tension

PET : Positron Emission Tomography

rCBF : Regional cerebral blood flow

rCMRg : Regional metabolic rate for glucose

$rScO_2$: Regional cerebral oxygenation

SD : Standard deviation

$SjvO_2$: Jugular venous oxygen saturation

TCD : Transcranial doppler

THI : Total haemoglobin index

TIVA : Total intravenous anesthesia

TOI : Tissue oxygen index

VIMA : Volatile induction and maintenance anaesthesia

XeCT : Xenon-enhanced computed tomography

ABSTRACT

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Title:

"A COMPARISON OF THE EFFECT OF ANAESTHESIA WITH SEVOFLURANE AND PROPOFOL ON CEREBRAL OXYGENATION DURING HYPERVENTILATION IN PATIENTS UNDERGOING SUPRATENTORIAL TUMOUR EXCISION – A RANDOMISED CONTROLLED STUDY"

Background:

The patients undergoing supratentorial tumour excision are often hyperventilated to reduce intracranial pressure (ICP), which can cause a reduction in cerebral blood flow (CBF) and cerebral oxygenation. Since intravenous and inhalational anaesthetic agents have different effects on cerebral haemodynamics, we aimed to compare cerebral oxygenation using Near Infrared Spectroscopy (NIRS) with sevoflurane or propofol at normocarbia and during hyperventilation in patients undergoing supratentorial tumour excision.

Materials and methods:

In this prospective randomised controlled single-blinded study, 50 patients were randomised into two groups. Group S received sevoflurane, and Group P received propofol for induction and maintenance of anaesthesia titrated to a Bispectral Index (BIS) value of 45-55. The cerebral oxygenation (rSO_2) values were taken from the bilateral forehead NIRS electrodes at baseline, at normocarbia

and hypocarbia in both groups. The mean between the two groups and between baseline, normocarbia ($PaCO_2$ 36-38mmHg) and hypocarbia ($PaCO_2$ 30mmHg) were compared on the tumour and the normal side using unpaired t-test and repeated measures ANOVA test, respectively. A p-value of <0.05 was considered significant.

Results:

Hypocarbia caused a reduction in rSO_2 values in both groups, but it was statistically significant in Group P. In the sub-group analysis of frontal glioma cases, in both the groups, a statistically significant decrease in the rSO_2 was noted during hypocarbia ($p<0.05$). When the rSO_2 values of the tumour side and normal side were analysed separately, the decrease in the rSO_2 values at hypocarbia was more in the P group (65.64 ± 4.26 vs 61.44 ± 4.78, $p<0.05$) on the normal side. There was no change in rSO_2 values on the tumour side.

Conclusion:

Hyperventilation can reduce cerebral oxygenation in patients with supratentorial tumours. This change was seen more with propofol and on the normal side, with no change in rSO_2 on the tumour side. Close monitoring for cerebral desaturation is needed in neurosurgical patients when administering hyperventilation to reduce ICP, especially when using total intravenous anaesthesia (TIVA).

INTRODUCTION

INTRODUCTION

Preventing cerebral ischaemia by ensuring adequate cerebral perfusion and oxygenation is one of the essential goals of neuroanaesthesia. Close monitoring of systemic and central nervous system function is required in the perioperative and critical care management of patients with neurologic disease. Maintaining hemodynamic stability, sufficient cerebral perfusion pressure (CPP), and cerebral oxygenation are essential factors to consider during neurosurgical anaesthesia. NIRS can provide an easy to use, non-invasive, continuous, real-time indirect assessment of CBF, which will be helpful intraoperatively, especially while administering hyperventilation along with TIVA to reduce ICP during supratentorial tumour surgeries.

Adequate cerebral oxygenation improves neurologic and surgical outcomes (1). The equilibrium between cerebral oxygen delivery and utilisation is assessed through cerebral oxygenation monitoring. Early postoperative cognitive dysfunction (POCD) has been linked to cerebral oxygen desaturation during surgery, which has been associated with delirium and longer hospitalisation in the elderly (2).

The anaesthetic technique used is indeed a factor that influences cerebral oxygenation. Propofol, being a cerebral vasoconstrictor and sevoflurane, being a cerebral vasodilator, can have varying effects on cerebral physiology. Valencia et al. while measuring rSO_2 using NIRS in patients undergoing general surgical procedures. Sevoflurane maintains rSO_2 better than propofol, according to their findings (3).

Hyperventilation is a common intervention employed during the anaesthetic management of supratentorial tumour excision. It is known to cause vasoconstriction of cerebral blood vessels, which reduces cerebral oxygenation. Dewhirst et al., in their study using NIRS, found that rSO_2 declined during general anaesthesia during hypocarbic conditions (4).

We could not find any study in the literature, that assess the combined effects of TIVA and inhalational anaesthesia on cerebral oxygenation during hyperventilation in neurosurgical patients. Hence, we planned to evaluate the same in our study.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Neurosurgical procedures and the various anaesthetic agents used, exert a complex effect on the systemic and cerebral circulations and may affect CBF, oxygenation and cerebral haemodynamics. Cerebral oxygenation depends upon adequate CBF and cerebral oxygen demand. The choice of anaesthetic technique may be a variable that can influence cerebral oxygenation and the long term outcome of patients. Adequate cerebral oxygenation has been associated with better outcomes in terms of neurologic and significant organ morbidity in various surgical scenarios (1).

MONITORING OF CEREBRAL OXYGENATION

Monitoring of cerebral oxygenation is an essential component of multimodality neuromonitoring. Various techniques have been employed for the early detection of perioperative cerebral ischemia and hypoxia, like brain tissue oxygenation ($PbtO_2$) and Jugular venous oxygen saturation ($SjvO_2$) measurements. However, these techniques are invasive or may require expertise, a learning curve and trained personnel. Cerebral NIRS is increasingly used to monitor rSO_2, which provides a non-invasive indirect assessment of CBF. The normal value for rSO_2 is between 60% and 70% (5). Cerebral oximetry can provide information on oxygen delivery and utilisation, allowing us to assess whether a patient has tissue hypoxia despite having normal systemic arterial saturation and blood pressure.

Principle of cerebral oximetry

Cerebral oximetry by NIRS is non-invasive optical technology to monitor CBF and cerebral perfusion. NIRS is based on optical spectrophotometry principles, taking the fact that most biological tissues, including the skull, are generally transparent to light in the NIR spectrum. The optodes, positioned on the forehead above the brow, transmit infrared light through the skull, penetrating the frontal cortex by several centimetres (Figure 1). The beam, which travels in a curved trajectory, is modulated by absorption and scatter, and reflected photons are captured by surface detectors (5). Most commercially available systems use reflectance-mode NIRS, with receiving optodes placed ipsilateral to the transmitter, because of the low signal-to-noise ratio due to the low intensity transmitted light. This design takes advantage of photons travelling in an elliptical path through a sphere, with the mean penetration depth proportional to the transmitter-receiver distance (Figure 2).

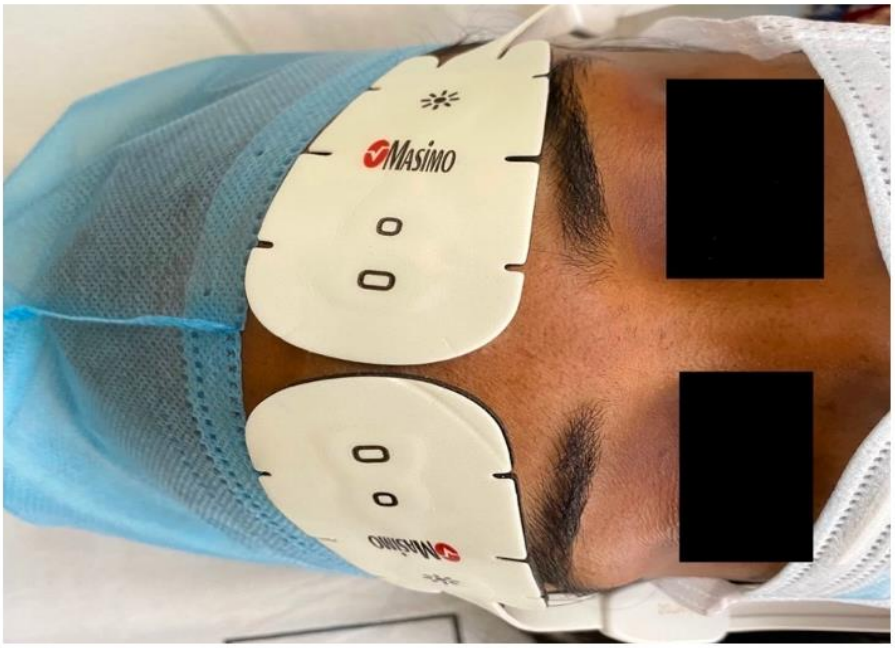

Figure 1: The positioning of NIRS electrodes on the forehead.

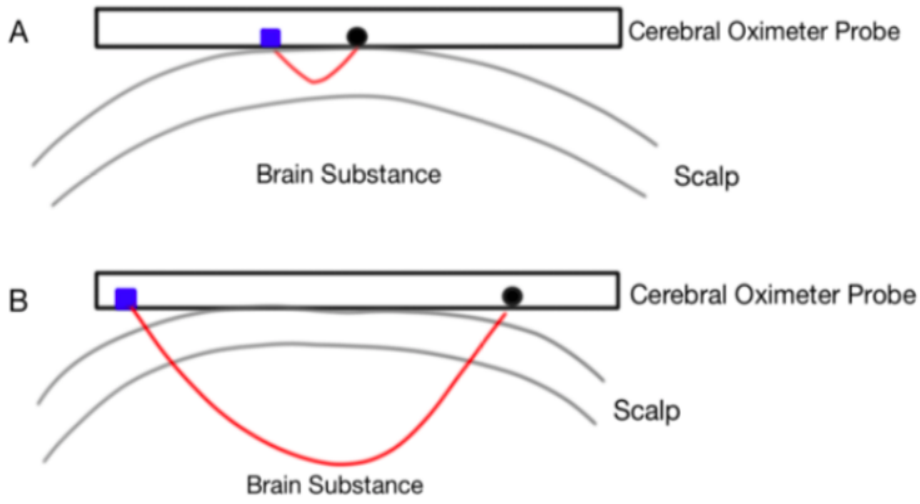

Figure 2 : Elliptical path of photon penetration

In the 700–1300 nm range, NIR light penetrates several centimetres in the biological tissue (6). Haemoglobin, bilirubin, and cytochrome are the primary light-absorbing molecules in tissue in the NIR range. The absorption spectra of deoxyhaemoglobin (Hb) is from 650 to 1000 nm, oxyhaemoglobin (HbO_2) from 700 to 1150nm, and cytochrome oxidase aa3 (Caa3) from 820 to 840 nm (7). The commercial devices utilise wavelengths of NIR light between 700 and 850 nm where the absorption spectra of Hb and HbO_2 are maximally separated, and there is minimal overlap with H_2O causing an alteration in the reflected NIRS signal. The differential absorption of NIR light by Hb and HbO_2 and the concentration of the same in the brain tissue form the basis of estimating brain oxygen saturation.

Cerebral oximeters calculate rSO_2 using the Beer-Lambert Law (8). Beer's law states that the intensity of transmitted light decreases exponentially as the concentration of a substance the light passes through increases, as shown in figure 3. Lambert's law states that the intensity of transmitted light decreases exponentially as the distance travelled by the light through a substance increases (figure 4). Measurement of tissue oxygen saturation and tissue haemoglobin content is determined by the difference in intensity between the transmitted and received light delivered at specific wavelengths as stated by the Beer-Lambert law above.

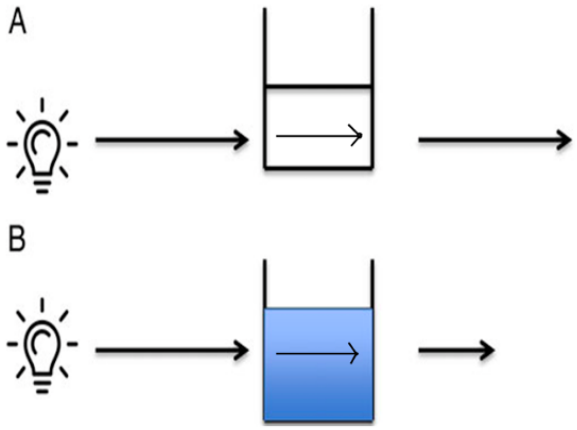

Fig 3: Beer's law (intensity of transmitted light decreases exponentially as the concentration of the solute increases)

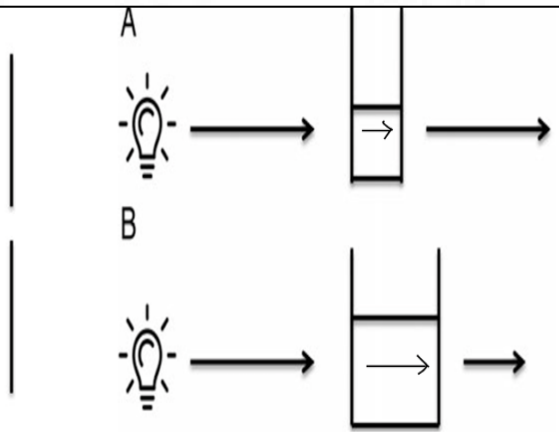

Fig 4 : Lambert's law (intensity of transmitted light decreases exponentially as the distance travelled by the light increases)

Most of the devices are continuous wave (CW) monitors with a transmitter-detector distance of 4 cm or less, allowing deeper cortical responses to be isolated from superficial extracranial signals (6). The CW devices use the red: infrared ratio to calculate haemoglobin saturation rather than measuring absolute Hb and HbO_2 levels. Optimising emitter-to-detector spacing, employing numerous wavelengths and detectors, or measuring absolute chromophore values are all ways to improve spatial resolution. The time domain and frequency domain (FW) techniques estimate rSO_2 using absolute values of oxygenated, deoxygenated, and total haemoglobin and account for variations in cerebral blood volume (9). To determine tissue oxygen index (TOI) and total haemoglobin index (THI), the FW-NIRS devices use a mathematical formula on photon diffusion theory.

Extracranial contamination can occur during NIRS monitoring. Skull thickness, optical path length, cerebro spinal fluid (CSF) layer, and haemoglobin content affect rSO2 values. This is subject to change due to technical differences in various gadgets (10).

Correlation of NIRS with cerebral oxygenation and CBF

Pollard et al. developed an algorithm based on the correlation between the cerebral oximetry values using NIRS and the estimated brain haemoglobin oxygen saturation ($SjvO_2$). There was a close association between rSO_2 and $SjvO_2$. They concluded that continuous cerebral oximetry might detect a reduction in brain oxygenation during systemic hypoxaemia (11).

Meeri et al. assessed CBF by diffuse correlation spectroscopy (DCS) and Hb, HbO2 measurement by NIRS. DCS/NIRS based CBF and frontal lobe oxygenation were compared along with xenon-enhanced computed tomography (XeCT) in patients at varying blood pressure and $PaCO_2$. Relative CBF measured by DCS ($rCBF_{DCS}$), and changes in HbO_2 (ΔHbO_2), Hb (ΔHb), and total haemoglobin concentration (ΔTHC), measured by NIRS, were continuously monitored throughout XeCT at baseline repeated after the intervention. $rCBF_{DCS}$ and $rCBF_{XeCT}$ showed good correlation among the patients. A moderate correlation was found between $rCBF_{DCS}$ and $\Delta HbO_2/\Delta THC$. NIRS and DCS were able to independently distinguish the effects of xenon inhalation on CBF. The authors concluded that DCS measurements of CBF measured with DCS and tissue blood oxygenation with NIRS provide a non-invasive, continuous bedside monitoring of CBF in neurocritical care patients (12).

The specific absorbance patterns of Hb and HbO_2 to NIR light are compared to determine rSO_2 of the frontal brain (13). As CBF drops, tissue oxygen extraction rises to maintain brain metabolism, resulting in a decline in haemoglobin saturation. Thus, rSO_2 is an indirect measure of CBF and an "index" of organ ischemia in the context of a steady metabolic rate (14). Monitoring rSO_2 allows for detecting clinically silent events of cerebral ischemia, and the technology has been utilised extensively in various settings, including adult surgery and neonatal intensive care. Many parameters, including haematocrit, hemoglobin-O_2 binding affinity, inspiratory oxygenation, and ventilation, can influence oxygen delivery and cerebral oxygen saturation (15).

Advantages and Limitations of NIRS

NIRS has numerous advantages, such as being non-invasive, the ability to simultaneously sample multiple regions of interest with a high temporal resolution, and being user-friendly. The most significant benefit of NIRS is its simplicity of usage; placing two oximeter probes on the forehead is fast and straightforward.

Though NIRS has multiple advantages, it is not without limitations. NIRS values can be confounded by several factors, such as contamination from extracerebral blood from the scalp or subdural hematoma, presence of non-heme tissue chromophores etc. The spatial resolution provided by NIRS is restricted. It can sense the outer 1-4 mm of the cortical surface only (16). Only the regional oxygen saturation is measured, not the global oxygenation (10). The use of diathermy, or electrosurgical equipment, can impact its accuracy. Also, the area between the light emitter and detector only contributes to the NIRS value (17). Blood from extracranial sources gives false low values. The rSO_2 measurements of different devices vary wildly, and the sensors and devices are not interchangeable. NIRS measurement is validated only for the frontal oxygenation changes.

EFFECTS OF ANAESTHETICS ON CEREBRAL OXYGENATION

The various anaesthetic agents exert a complex effect on the systemic and cerebral circulations through direct effects on the vessels and modulation of the endogenous regulatory mechanisms. The choice of anaesthesia can play a fundamental role in patient outcomes. The alteration of cerebral haemodynamics by anaesthetic agents can influence brain tissue oxygenation during neurosurgical

procedures. The intravenous and inhalational agents have different effects on CBF and oxygenation. For these reasons, it is necessary to understand the impact of these anaesthetics on cerebral haemodynamics (18).

Effects of Propofol on Cerebral Circulation

Propofol reduces global CBF by 50-60% mainly due to its metabolic depressant effect (19). Overall metabolism in the cortex is depressed more than in the subcortical brain areas. This variation in regional CBF (rCBF) reduction has been confirmed with Positron Emission Tomography (PET) studies which demonstrated a large preferential decrease in the medial thalamus, cuneus and precuneus, and posterior cingulate, orbitofrontal, and right angular gyri (20). The metabolism in the cerebral cortex decreases (by 58%) more than in the sub-cortical brain areas (by 48%). In patients with intracranial tumours, ICP was shown to be lower and CPP higher in patients anesthetised with propofol when compared with those anesthetised with volatile anaesthetics (21).

Effects of Sevoflurane on Cerebral Circulation

The inhalational anaesthetics are concentration-dependent cerebral vasodilators. High concentrations of inhalational anaesthetics cause direct vasodilation resulting in a higher CBF/$CMRO_2$ ratio (22). They have got both CMR suppression and intrinsic cerebral vasodilatory effect. At a dose of 0.5 MAC (minimum alveolar concentration), there occurs a reduction in CBF due to CMR suppression. At 1 MAC, vasodilatory effects and CMR are in balance. Beyond 1 MAC, the vasodilatory effect predominates, and CBF significantly increases.

During sevoflurane anaesthesia, the global CBF remains, and cerebral autoregulation remains unaltered up to 1.5 MAC. The rCBF response is heterogeneous, increasing the anterior cingulate and decreasing the cerebellum. The flow-metabolism coupling is preserved during anaesthesia with sevoflurane. It decreases rCMRg (regional metabolic rate for glucose) in all regions of the brain, more in the occipital lobe (by 68%), thalamus (by 68%) and the lingual gyrus (by 71%) (23).

Using PET, the study by Kaisti et al. showed either a decrease or no change in global CBF occurred with sevoflurane (24). In this investigation, MAP was found to be considerably lower with sevoflurane, and as long as MAP is maintained, sevoflurane does not affect the CBF.

Comparison of the effects of sevoflurane and propofol on cerebral oxygenation

Ruzman et al. studied the effects of volatile induction and maintenance anaesthesia with sevoflurane (VIMA) and total intravenous anaesthesia with propofol (TIVA) on rSO_2 in patients during laparoscopic cholecystectomy. In all time points throughout induction, CO_2 insufflation, and recovery, the VIMA group had statistically higher rSO_2 levels than the TIVA group. Critical rSO_2 declines were statistically less prevalent in the VIMA group ($P<0.05$). In addition, VIMA exhibited a much lower number of critical rSO_2 decreases (25).

Using cerebral oximetry, Kim et al. investigated the effects of propofol and sevoflurane anaesthesia on brain oxygenation in gynaecological laparoscopic

surgery. They discovered that propofol had considerably reduced rSO_2 values during pneumoperitoneum in the Trendelenburg position and following desufflation of the abdomen in the neutral position (26).

Park et al. investigated the impacts of sevoflurane and propofol on rSO_2 in carotid endarterectomy patients. Before carotid artery clamping, the mean value of the relative changes in rSO_2 was significantly higher, and the maximal decrease in rSO_2 was lower in the sevoflurane group compared with the propofol group in the contralateral (normal) site. But, there was no difference in the ipsilateral (affected) site. Although rSO_2 reduced after carotid artery clamping and increased after declamping, the difference between the two groups was insignificant (27).

HYPERVENTILATION

The patients undergoing supratentorial tumour excision are often hyperventilated to reduce ICP. Hyperventilation is also recommended to manage raised ICP intraoperatively and in neurointensive care. It leads to cerebral vasoconstriction-related reduction of the cerebral blood volume (CBV), one of the components of the intracranial contents; thereby, it decreases ICP and relaxes the brain. There is a linear response of CBF to $PaCO_2$ between 20 and 80mmHg. Hypocapnia can cause a decrease in cerebral oxygenation by vasoconstriction in cerebral blood vessels, which decreases the CBV and CBF. The Brain Trauma Foundation recommends using a cerebral oxygenation monitor while instituting hyperventilation to reduce ICP (28).

Reinstrup et al. evaluated CBF, TCD flow velocity measurements and cerebrovascular reactivity to hypocapnia in patients with acute TBI. In patients undergoing hematoma evacuation under general anaesthesia, measurements were taken during normocapnia and hypocapnia (29). According to the researchers, hypocapnia resulted in a significant decrease in TCD-mean flow velocity and CBF reduction.

Dewhirst et al. studied changes in cerebral oxygenation based on intraoperative Ventilation strategy. They monitored rSO_2 using NIRS during normocarbia (35-40 mmHg) with a low fraction of inspired oxygen (FiO_2) of 0.3 , hypocarbia (25-30 mmHg) and low FiO_2 of 0.3 , hypocarbia and a high FiO_2 of 0.6; and normocarbia and a high FiO_2. They found that during general anaesthesia, brain oxygenation decreased slightly with hypocarbia. Hypocarbia induced reduction in rSO_2 levels was quickly reversed with supplemental oxygen (60% vs 30%) and returned to baseline levels (4).

Heine M et al. studied the influence of cardiopulmonary changes on cerebral oxygenation, as assessed by NIRS. They proposed that near-maximal exercise intensity cerebral deoxygenation is mediated by hyperventilation through hypocapnia-induced CBF decreases (30).

Meng L et al. compared the effects of moderate hyperventilation on $SjvO_2$, cerebral oxygen extraction ratio (O_2ER) in patients with supratentorial tumours under Propofol and Isoflurane anaesthesia. This was a cross over study in which the patient received propofol based anaesthesia, and following a stabilisation period of 30 minutes, they got isoflurane anaesthesia. The next group received the

same drugs in the reverse order. The changes in the arterial and jugular bulb blood gases were noted. They found that the mean $SjvO_2$ value significantly decreased, and the O_2ER significantly increased under isoflurane and propofol anaesthesia during hyperventilation. These changes were more pronounced under propofol anaesthesia (31).

These studies have demonstrated the need for close monitoring for cerebral desaturation in neurosurgical patients, especially when administering hyperventilation for reducing intracranial pressures. It is better to use a non-invasive method of cerebral oximetry like NIRS, which can be routinely used in all craniotomies for supratentorial tumour excision.

HYPOTHESIS

HYPOTHESIS

Null hypothesis:

Cerebral oxygenation will not change during hyperventilation with Sevoflurane or Propofol anaesthesia in patients undergoing supratentorial tumour excision.

Alternate hypothesis:

Cerebral oxygenation is better with sevoflurane than propofol during hyperventilation in patients undergoing supratentorial tumour excision.

AIMS AND OBJECTIVES

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Aim:

To compare cerebral oxygenation (rSO_2) between patients receiving sevoflurane or propofol at normocarbia and during hyperventilation for supratentorial tumour excision using Near Infrared Spectroscopy (NIRS).

MATERIALS AND METHODS

MATERIALS AND METHODS

We conducted a prospective single-blinded randomised controlled study to assess the changes in cerebral oxygenation during hyperventilation with Sevoflurane or Propofol anaesthesia in patients undergoing supratentorial tumour excision in the Neuro-Surgical Operation Theatre (NSOT) of Sree Chitra Tirunal Institute of Medical Sciences and Technology (SCTIMST), Trivandrum, which is a specialised tertiary referral centre.

After approval by Institutional Ethics Committee (SCT/IEC/1565/OCTOBER-2020, IEC Regn No. ECR/189/Inst/KL/2013/RR-16, dated 30.10.2020, Appendix - b) and CTRI registration (CTRI/2021/10/037506) our study was conducted between December 2020 to November 2021.

Inclusion criteria:

- Consenting adult patients undergoing elective supratentorial tumour excision
- Age 18-60yrs
- ASA (American Society of Anaesthesiologists) class 1 and 2
- GCS 15 prior to the surgery

Exclusion criteria:

- Patient refusal
- Age<18yrs, >60yrs

- Patients with a difference of 10% or more in the baseline NIRS values between right and left sides
- Patients with clinical signs (headache, vomiting, confusion, papilledema, pupillary asymmetry) or radiological signs (midline shift>1cm, presence of hydrocephalus) of raised intracranial pressure preoperatively
- Patients with carotid artery disease
- Long-standing uncontrolled diabetes mellitus, systemic hypertension, cardiovascular disease, COPD
- Patients with a previous history of stroke, transient ischemic attacks
- Obesity
- ASA class III or higher patients.
- Patients with subarachnoid haemorrhage, vasospasm.
- Pregnant & nursing mothers.

Recruitment:

The Principal investigator and Co-Principal Investigators screened the patients for recruitment to the study based on the inclusion and exclusion criteria. The eligible participants were informed about the study, and an informed consent was obtained from the patient or the patient's legal representatives. The participants were randomised into two groups (Group P- propofol group, Group S – sevoflurane group) before the commencement of the study by computer-

generated random table and allocation concealed by sealed envelope technique. The patients were blinded about the anaesthetic technique. A technician who was not a part of the study noted down the values of rSO_2.

No sedative/opioid premedication was given. Patients were taken up for surgery with standard monitoring, including Electrocardiography (ECG), Pulse oximetry, Non-invasive blood pressure monitoring and baseline values were noted. rSO_2 was monitored with bilateral NIRS sensors on the forehead, and BIS monitoring with BIS electrode on the forehead. Bilateral rSO_2 readings were taken, and if there was a difference of 10% or more between the two sides' values, the subject was excluded from the study. rSO_2 values of both sides at a FiO_2 of 0.5 were set as the baseline.

Patients were pre oxygenated for 3minutes with FiO_2 of 1.0. Group S patients were induced and maintained with sevoflurane, starting at 8% and gradually reducing the concentration titrated to a BIS value of 45-55. Group P patients were induced and maintained with target-controlled infusion (TCI) of propofol with Schneider model with effect-site concentration starting at 4mcg/ml and reducing the concentration at the point of loss of verbal response. All patients were given Inj. Fentanyl 2 mcg/kg and Inj. Vecuronium 0.1 mg/kg and the trachea was intubated with an appropriate sized endotracheal tube. Anaesthesia was maintained using a combination of Oxygen/Air (FiO_2 0.5) and the study drug to maintain a BIS of 45-55. The patients were ventilated with volume-controlled mode of ventilation titrated to an $EtCO_2$ of 35mmHg and were maintained for 15minutes. A baseline arterial blood gas analysis (ABG) was done, $PaCO_2$ and

$PaCO_2$ – $EtCO_2$ gradient was noted, and mechanical ventilation was adjusted to a $PaCO_2$ between 36-38mmHg (defined as normocarbia). The NIRS values were noted at this point. Then the respiratory rate was increased targeted to a $PaCO_2$ of 30mmHg (defined as hypocarbia) for 15minutes, and ABG was done to confirm it, and NIRS value at this point was noted. Then the ventilation was adjusted back to steady-state, and the surgery was allowed to start. MAP was maintained within 20% of the baseline values throughout the procedure using boluses of mephentermine.

Figure 5: NIRS values recorded at baseline, normocarbia and hypocarbia

Data collection and Observations:

Baseline heart rate MAP, SpO_2, and BIS were measured. Baseline bilateral rSO_2 values were taken. Haemodynamic parameters, $EtCO_2$, BIS value and rSO_2 by NIRS were noted before induction, at normocarbia and at hypocarbia. MAP was kept within 20% of baseline values, and the number of boluses of mephentermine administered was noted. The MAC of sevoflurane in Group S patients and the effect-site concentration of propofol in Group P patients required to maintain BIS of 45-55 were recorded at normocarbia and at hypocarbia.

STATISTICAL ANALYSIS

Sample Size Calculation

The normal range of rSO_2 was assumed to be 60-70. A change of 20% of this average value was considered a margin of equivalence. Assuming a 5% significance level and 80% power, the required number of participants were calculated as 25 per group. We included 96 patients in the study, considering the possibility of dropouts.

Statistical Methods

Data were manually entered into the proforma. The collected data were analysed with SPSS software (version 26.0). The normality of the data was tested using the Shapiro-Wilk test. Continuous variables were expressed as Mean ± Standard deviation (SD), and Categorical data were described in terms of number and percentage. The rSO_2 between the two groups at baseline, normocarbia and hypocarbia, was compared using an unpaired t-test. The values within a group during baseline, normocarbia and hypocarbia were compared with repeated measures ANOVA test. A p-value of <0.05 was considered significant.

RESULTS AND OBSERVATIONS

RESULTS AND OBSERVATIONS

We screened 96 patients with supratentorial tumours for the study, from which 57 patients were recruited based on inclusion and exclusion criteria. 7 patients with a difference of >10% in the baseline rSO_2 between both sides were excluded, and the study was completed in 50 patients without any dropouts. The data of 50 patients were finally analysed in the study; 25 patients were enrolled in each group (Fig. 6).

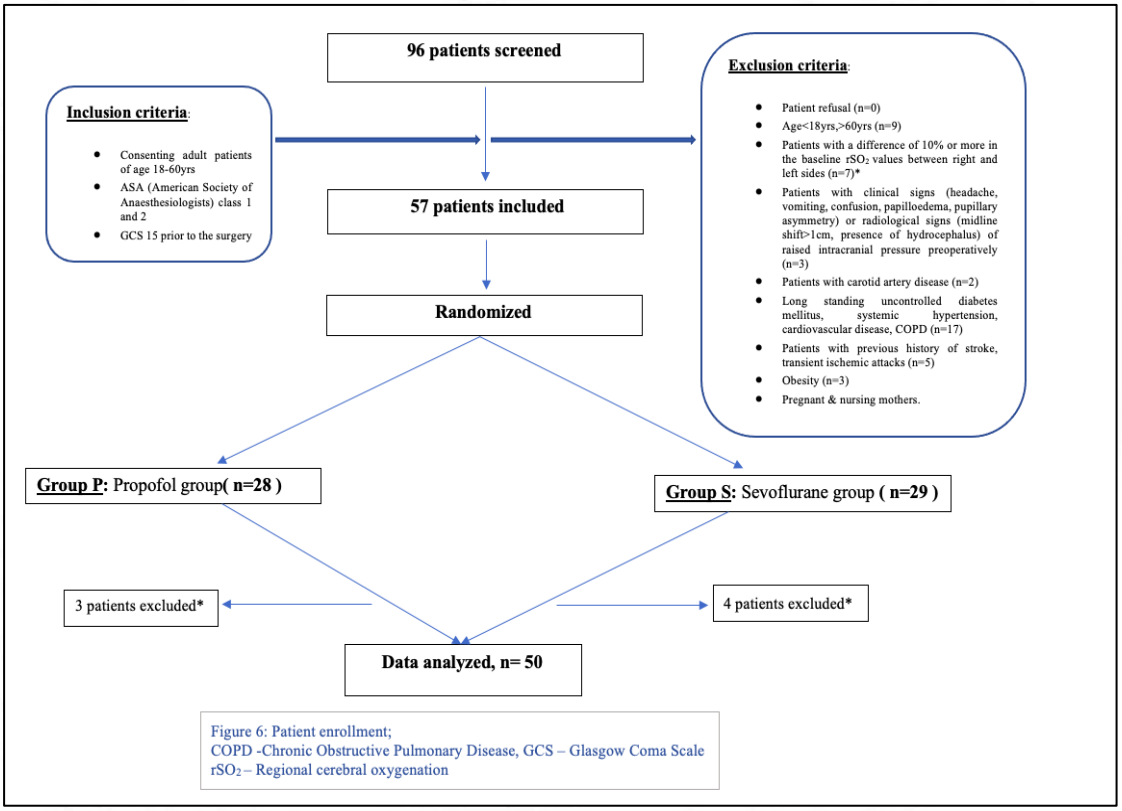

Figure 6: Patient enrollment;
COPD -Chronic Obstructive Pulmonary Disease, GCS – Glasgow Coma Scale
rSO_2 – Regional cerebral oxygenation

1) Demographic details of study participants

The demographic parameters of the study population were analysed. The results were as follows:

Table1: Demographic characteristics of study population

Parameter assessed			Group P (n=25)	Group S (n=25)	P value (inter group)
Age (years)			43.16 ± 12.78	46.2 ± 11.81	0.21
Males			68%	68%	1
ASA 1			76%	52%	
Left sided tumour			15 (60%)	11 (44%)	
Size of tumour (cc^3)			51.28 ± 45.08	48 ± 40.10	0.78
Anaesthetic concentration	MAC	Normocarbia		1.11 ± 0.12	
		Hypocarbia		0.98 ± 0.10	
	Effect site concentration (mcg/ml)	Normocarbia	3.59 ± 0.37		
		Hypocarbia	2.89 ± 0.37		
BIS value		Normocarbia	47.8 ± 2.37	47.55 ± 1.54	0.58
		Hypocarbia	47.34 ± 2.11	46.64 ± 1.81	0.21

Table 1: Comparison of the demographic variables between the two groups. Continuous variables were expressed as Mean ± Standard deviation (SD) and Categorical data are described in terms of number and percentage. Inter-group analysis was done using unpaired t test. A p value of <0.05 was considered significant. ASA: American Society of Anaesthesiologists; MAC: Minimum Alveolar Concentration; BIS: Bispectral Index

The demographic parameters were statistically comparable in both the study groups (Table 1). The target BIS value was attained with the anaesthetic concentration of 0.98 ± 0.10 MAC in Group S and effect-site concentration of 2.89 ± 0.37 in Group P during hypocarbia.

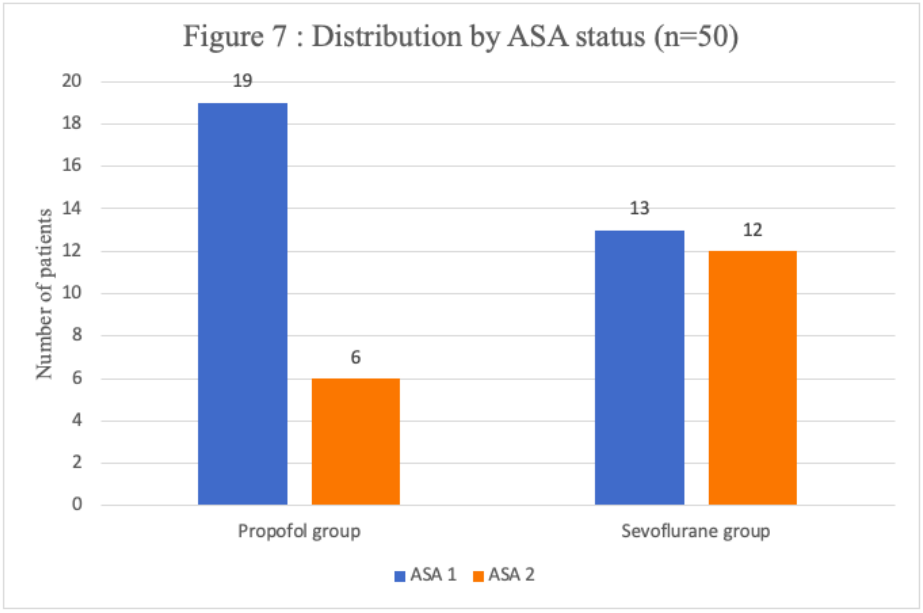

Figure 7 : Distribution of study groups with respect to ASA status

2) Diagnosis of enrolled cases

The data on the diagnosis of the study population was analysed. The results were as follows (Table 2, Fig 8):

Table 2: Diagnosis of enrolled cases in study groups		
	Group P (n=25)	Group S (n=25)
Frontal glioma	18 (72%)	17 (68%)
Temporal glioma	2 (8%)	5 (20%)
Parietal glioma	3 (12%)	2 (8%)
Lymphoma	0	1 (4%)
Meningioma	2 (8%)	0

Table 2 - diagnosis of enrolled cases in both groups, expressed as number and percentage

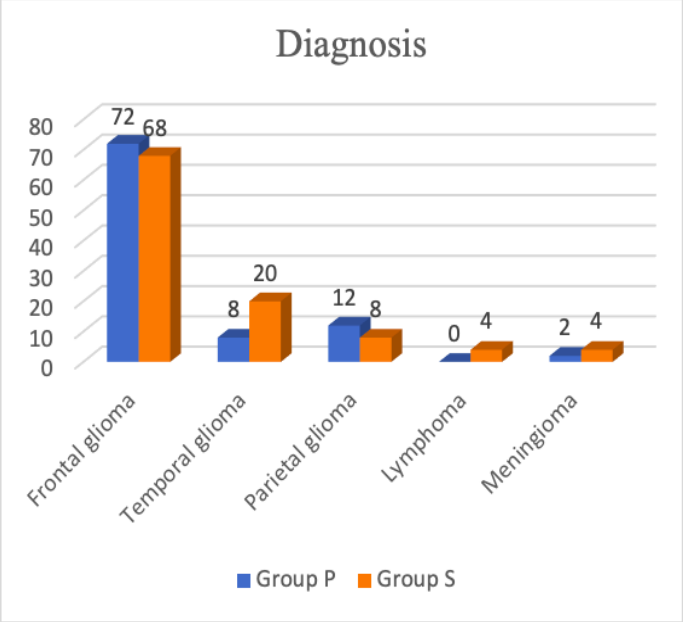

Figure 8 : Diagnosis of cases among study groups

72% in Group P and 68% in Group S were frontal gliomas. (Table 2, Figure 8). Both groups were comparable in terms of diagnosis.

3) Ventilatory parameters in the study population at various times of assessment

On evaluating the ventilatory parameters, viz. PaO_2, $EtCO_2$, $PaCO_2$ and Minute ventilation, we got the results as follows (Table 3):

Table 3: Ventilatory parameters in study groups in various phases (n=50)

Parameter	*Phase assessed*	*Propofol group (n=25)*	*Sevoflurane group (n=25)*	*P value (intergroup)*
PaO_2 (mmHg)	Normocarbia	243.68 ± 62.49	252.17 ± 49.37	0.21
	Hypocarbia	239.69 ± 63.41	245.81 ± 48.29	0.17
	P value (Intra-group)	0.19	0.12	
$EtCO_2$ (mmHg)	Normocarbia	32.36 ± 1.15	31.56 ± 1.33	0.45
	Hypocarbia	25.48 ± 1.42	24.96 ± 1.54	0.51
	P value (Intra-group)	**0.01**	**0.01**	
$PaCO_2$ (mmHg)	Normocarbia	37.39 ± 1.15	37.23 ± 0.85	0.76
	Hypocarbia	30.2 ± 0.94*	30.27 ± 0.62*	0.84
	P value (Intra-group)	**0.01**	**0.01**	
Minute ventilation (L/min)	Normocarbia	5.82 ± 0.58	6.02 ± 0.67	0.12
	Hypocarbia	7.44 ± 0.45	7.53 ± 0.74	0.08
	P value (Intra-group)	**0.01**	**0.01**	

Table 3 - The changes in ventilatory parameters at different time points in study groups. Continuous variables were expressed as Mean ± Standard deviation (SD). Inter-group analysis was done using unpaired t test. Intra-group analysis was done using repeated measures ANOVA test. A p value of <0.05 was considered significant*. $PaCO_2$: Partial pressure of carbon dioxide in arterial blood; EtCO2: end tidal carbon dioxide; PaO_2: Partial pressure of oxygen in arterial blood.

On evaluating the ventilatory parameters were found to be comparable between study groups. The $PaCO_2$ during normocarbia in Group P and Group S were 37.39 ± 1.15 and 37.23 ± 0.85, respectively. The $PaCO_2$ at hypocarbia in Group P and Group S were 30.2 ± 0.94 and 30.27 ± 0.62 respectively*.

4) Hemodynamic parameters in study groups

The analysis of the haemodynamic parameters of the study population revealed the following results (Table 4):

Table 4: Haemodynamic parameters in study groups at various phases (n=50)

Parameter	*Phase assessed*	*Propofol group (n=25)*	*Sevoflurane group (n=25)*	*p value (intergroup)*
Heart rate (beats per minute)	Baseline	68.16 ± 8.52	69.64 ± 8.45	0.58
	Normocarbia	66.56 ± 8.75	69.32 ± 7.98	0.31
	Hypocarbia	66.04 ± 8.16	67.48 ± 7.71	0.48
	P value (Intra-group)	0.49	0.39	
MAP (mmHg)	Baseline	84.32 ± 9.06	82.28 ± 8.99	0.47
	Normocarbia	80.44 ± 7.37	80.12 ± 5.6	0.78
	Hypocarbia	78.52 ± 7.41	80.92 ± 5.97	0.29
	p value (Intra-group)	0.19	0.57	
Number of Mephentermine boluses	Normocarbia	14	16	>0.05
	Hypocarbia	3	5	>0.05

Table 4 - the changes in Haemodynamic parameters at different time points in study groups. Continuous variables were expressed as Mean ± Standard deviation (SD). Inter-group analysis was done using unpaired t test. Intra-group analysis was done using repeated measures ANOVA test. A p value of <0.05 was considered significant. MAP: Mean arterial pressure

The mean heart rate and MAP were comparable between the study groups at all phases of assessment. No statistically significant change was noted on intra-group analysis in both study groups. (Table 4).

5) Cerebral oxygenation (rSO_2) assessment by NIRS in the study population

Table 5: Mean rSO_2 in study groups for average of both sides (n=50)

Phase assessed	Group P (n=25)		Group S (n=25)		p value (intergroup)
	Range	Mean value	Range	Mean value	
Before induction	60-75	68.76 ± 3.09	58-74	67.92 ± 3.78	0.55
FiO_2 0.5	62-75	69.7 ± 2.89	58-76	68.84 ± 3.67	0.52
Normocarbia	54-73	66.28 ± 3.5	62-72	67.14 ± 2.4	0.39
Hypocarbia	52-71	62.34 ± 3.78	52-70	64.82 ± 3.46	0.18
p value (Intra-group)		**0.03**		0.21	

Table 5: the changes in cerebral oxygenation values at various time points. Continuous variables were expressed as Mean ± Standard deviation (SD). Inter-group analysis was done using unpaired t test. Intra-group analysis was done using repeated measures ANOVA test. A p value of <0.05 was considered significant. FiO_2: Fractional inspired concentration of oxygen; rSO2: regional cerebral oxygen saturation

The average value of rSO_2 on both sides was analysed. These values were comparable between the study groups at all phases of assessment. **On intra-group analysis in the Propofol group, a statistically significant decrease in the rSO_2 was noted** (p-value 0.03). In the sevoflurane group, no statistically significant change was noted. (Table 5)

Since most of the cases were frontal gliomas, a sub-group analysis was done in the same, revealing the following results (Table 6).

Table 6: Mean rSO_2 in study groups for average of both sides in Frontal Gliomas (n=37)

Phase assessed	*Group P (n=19)*	*Group S (n=18)*	*p value (intergroup)*
Before induction	68.34 ± 3.28	67.08 ± 4.11	0.21
FiO2 0.5	69.5 ± 3.07	68.25 ± 4.13	0.31
Normocarbia	66.08 ± 3.76	67.11 ± 2.58	0.29
Hypocarbia	63.24 ± 3.78	64.81 ± 3.72	0.25
p value (Intra-group)	**0.03**	**0.04**	

Table 6 showing the changes in cerebral oxygenation values at various time points in patients in frontal tumours. Continuous variables were expressed as Mean ± Standard deviation (SD). Inter-group analysis was done using unpaired t test. Intra-group analysis was done using repeated measures ANOVA test. A p value of <0.05 was considered significant. FiO_2: Fractional inspired concentration of oxygen; rSO2: regional cerebral oxygen saturation.

On intra-group analysis in both the groups, statistically, a significant decrease in the rSO_2 was noted ($p<0.05$).

The rSO2 values for tumour and normal sides were analysed separately in each group. The results are as follows (Fig 9, Table 7):

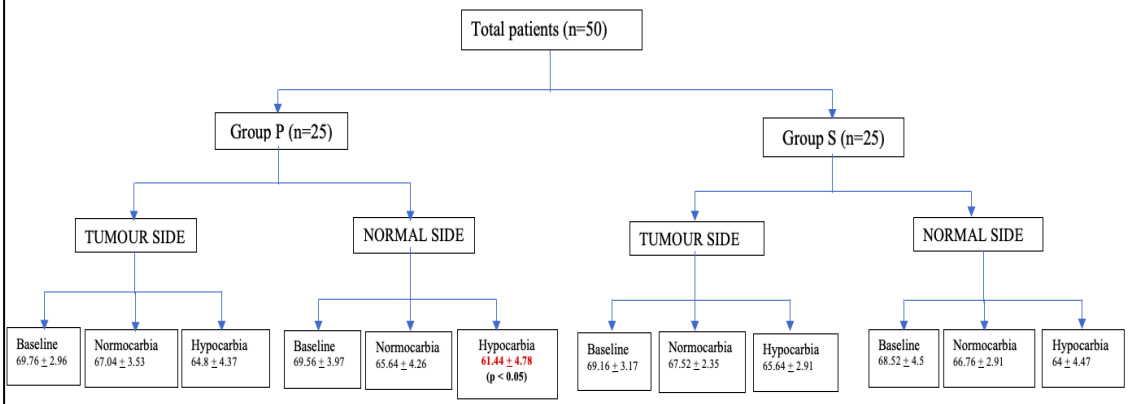

Fig 9: Flow chart showing the changes in cerebral oxygenation values at various time points.

Table 7: Mean rSO_2 in study groups in various phases (n=50)

	Normal side			Tumour side		
Phase assessed	*Group P (n=25)*	*Group S (n=25)*	*P value (intergroup)*	*Group P (n=25)*	*Group S (n=25)*	*p value (intergroup)*
Before induction	68.64 ± 3.99	67.68 ± 4.68	0.61	68.84 ± 3.26	68.16 ± 3.15	0.71
FiO2 0.5	69.56 ± 3.97	68.52 ± 4.5	0.37	69.76 ± 2.96	69.16 ± 3.17	0.65
Normocarbia	65.64 ± 4.26	66.76 ± 2.91	0.58	67.04 ± 3.53	67.52 ± 2.35	0.49
Hypocarbia	61.44 ± 4.78	64 ± 4.47	0.11	64.8 ± 4.37	65.64 ± 2.91	0.52
p value (Intra-group)	**0.04**	0.19		0.26	0.41	

Table 7: the changes in rSO_2 values at various time points on normal side and tumour side separately. Inter-group analysis was done using unpaired t test. Intra-group analysis was done using repeated measures ANOVA test. A p value of <0.05 was considered significant. FiO_2: Fractional inspired concentration of oxygen; rSO_2: regional cerebral oxygenation

On intra-group analysis in the Propofol group, a statistically significant decrease in the rSO_2 was noted at hypocarbia on the normal side ($p<0.05$). On intra-group analysis in both study groups, no statistically significant change was noted on the tumour side.

DISCUSSION

DISCUSSION

The anaesthetic agent used can impact cerebral oxygenation and, as a result, the outcome of neurosurgery procedures. Cerebral oxygenation represents the amount of oxygen available for consumption and energy metabolism in the cerebral tissue. Besides, rSO_2 measurement by NIRS gives an indirect assessment of CBF.

There exists a linear response of CBF to $PaCO_2$ between 20 and 80mmHg. Controlling $PaCO_2$ by transient hyperventilation is a common strategy in the anaesthetic management of patients undergoing supratentorial tumour excision or other neurosurgical emergencies to reduce intracranial pressure. This may drop CBV, one of the intracranial components, resulting from cerebral vasoconstriction, lowering ICP.

Our study results found that the rSO_2 values at baseline were comparable between the 2 groups. One patient in Group P had rSO_2 values below 55 during normocarbia.

Our results were similar to another study by Valencia et al., who compared the effect of sevoflurane and propofol on cerebral oxygenation in patients undergoing general surgical procedures. The researchers found no significant differences between the groups in minimum, mean, or maximum rSO_2. Propofol anaesthesia had a more substantial reduction in rSO_2 than sevoflurane anaesthesia. They concluded that sevoflurane preserved cortical rSO_2 measured with NIRS better than propofol (3).

Jeong et al., in their study, compared the effects of anaesthetics on cerebral oxygenation during surgery in beach chair position (BCP), using $SjvO_2$ and rSO_2. They found that the episodes of reduced $SjvO_2$ were more in the P/R group during BCP. However, there was no significant difference between the two groups in the incidence of rSO2 reduction. They could not find any correlation between $SjvO_2$ and rSO_2. Their study group had more elderly subjects (65 ± 9 years) with higher ASA grades. But the study population in our study was ASA 1 & 2 patients in the lower age group (32). In our study, we could pick up one episode of desaturation during normocarbia even with supine position. So, the presence of an intracranial space-occupying lesion can influence rSO_2 values.

Hyperventilation is known to cause a decline in cerebral oxygenation. In our study, there was a reduction in rSO_2 during hypocarbia in both the groups, but it was statistically significant only in Group P patients. During hypocarbia, the rSO_2 values varied from 52-71 in Group P, and 52-70 in Group S. Critically low values (<55) were more in Group P.

Since commercially available NIRS monitors calculate rSO_2 of frontal regions, we recruited more frontal gliomas. A sub-group analysis showed that hypocarbia reduced rSO_2 values in both the study groups with statistical significance.

Dewhirst et al. studied the impact of intraoperative ventilation strategy on cerebral oxygenation. They monitored rSO_2 using NIRS during both normocarbia (35-40 mmHg) and hypocarbia with a low (0.3) fraction of inspired oxygen (FiO_2) and a high FiO_2 (0.6). They concluded that cerebral oxygenation

declined with general anaesthesia during hypocarbic conditions. The oxygen administration at FiO_2 0.6 reversed the hypocarbia induced reduction in rSO_2 (4). We did not assess the rSO_2 values during low FiO_2 as in our study, it was standardised at 0.5 at all time points. Even with a FiO_2 of 0.5, we got reduced rSO_2 values during hypocarbia.

Meng L et al. compared the effects of moderate hyperventilation on $SjvO_2$ and cerebral oxygen extraction ratio (O_2ER) in patients with supratentorial tumours under Propofol and Isoflurane anaesthesia. This was a cross over study in which the patient received propofol based anaesthesia, and following a stabilisation period of 30 minutes, they got isoflurane anaesthesia. The next group received the same drugs in the reverse order. The changes in the arterial and jugular bulb blood gases were noted. They found that the mean $SjvO_2$ value significantly decreased, and the O_2ER significantly increased under isoflurane and propofol anaesthesia during hyperventilation. These changes were more pronounced under propofol anaesthesia (31).They used $SjvO_2$, which reflects the whole brain oxygenation, whereas we used rSO_2, which measures the regional cerebral oxygenation, mainly in the frontal region. Since they used $SjvO_2$, they could not assess the rSO_2 of the tumour side and normal side separately, which was addressed in our study.

When we analysed the rSO_2 on the normal side and tumour side separately, a statistically significant decrease in the mean rSO_2 was observed during hypocarbia ($p<0.05$) on the normal side in Group P alone. No statistically significant change was observed in both groups on the tumour side. We assume

that this observation can be due to impaired cerebrovascular reactivity (CVR), which can be seen in patients with intracranial space-occupying lesions. CVR changes in response to anaesthetic induction with propofol in patients with intracranial space-occupying lesions were studied by Schmieder et al. using bilateral TCD. CBF reduction after propofol was less pronounced on the side of the tumour (33).In our study, too, the decrease in rSO_2 was less apparent in the tumour side. The impairment of CVR in diffuse gliomas was assessed by Fierstra et al. with iso-oxic changes in CO_2. The patients with diffuse gliomas had impairment in both intralesional and whole brain CVR, which directly correlated with tumour volume (34).

Inhalational and intravenous anaesthetic agents have varying effects on CVR-CO_2. These effects have been studied in patients with intact cerebral autoregulation and CVR. The changes in cerebral oxygenation that occurs after the administration of anaesthesia and during varying $PaCO_2$ concentrations gives us a hint of the integrity of CVR. The previous studies demonstrate that CVR changes are better picked up by assessing CBF with TCD or specific MRI sequences. But in our study, we could appreciate this even with NIRS.

STRENGTHS AND LIMITATIONS OF THE STUDY

STRENGTHS OF THE STUDY

1. The first study in neurosurgical patients assessing cerebral oxygenation during the combined effect of anaesthetic agents and hyperventilation

2. Since NIRS mainly detects the changes in frontal regions, its reliability in our study was improved by the higher proportion of frontal gliomas.

3. Previous studies which demonstrated decreased rSO_2 with Propofol anaesthesia were done in non-neurosurgical elderly patients. Our study revealed the same even in young, healthy adult neurosurgical patients.

4. We assessed the rSO_2 changes in the tumour and normal sides separately, which was not done in previous studies.

5. We based our study on NIRS since it is an easy to use, non-invasive, continuous, real-time indirect assessment of CBF, which will be helpful intraoperatively.

LIMITATIONS OF THE STUDY

Our study has few following limitations:

1. NIRS only assesses the regional cerebral oxygenation, mainly of the frontal region. So, only a small area of the total intracranial compartment is covered. The higher proportion of frontal gliomas in our study has overcome this limitation.

2. The reduction in regional CBF with sevoflurane and propofol is variable, with propofol reducing CBF more in orbitofrontal, medial thalamus, cuneus and precuneus regions and sevoflurane in the lingual gyrus, occipital lobe and thalamus. This might have affected our study results.

3. The patients with features of raised ICP were not included in our study.
4. We did not evaluate the long term functional outcome of the patients. So, the clinical significance of the study is not validated. More research is needed to improve the validity of the findings.
5. Ours was a single centre study of a small sample size.

CONCLUSION

CONCLUSION

Our study found that hyperventilation reduced cerebral oxygenation in patients with supratentorial tumours, which was more marked with TIVA. The reduction in cerebral oxygenation was observed only on the normal side.

Close monitoring for cerebral desaturation is needed in neurosurgical patients when administering hyperventilation to reduce ICP, especially when using TIVA.

SUMMARY

SUMMARY

One of the major objectives of neuroanaesthesia is to prevent cerebral ischaemia by maintaining adequate cerebral perfusion and cerebral oxygenation. The anaesthetic technique may be a variable that can affect cerebral oxygenation. Propofol brings a cerebral vasoconstrictor and sevoflurane, being a cerebral vasodilator can vary cerebral physiology. Hyperventilation is a common intervention employed during the anaesthetic management of supratentorial tumour excision. It results in hypocarbia which can decrease cerebral oxygenation via cerebral vessels vasoconstriction. Hence, we aimed to compare cerebral oxygenation using Near Infrared Spectroscopy (NIRS) between patients receiving sevoflurane or propofol at normocarbia and hypocarbia in patients undergoing supratentorial tumour excision.

In this prospective randomised controlled single-blinded study, 50 patients were randomised into 2 groups. Group S received sevoflurane, and Group P received propofol for induction and maintenance of anaesthesia titrated to a Bispectral Index (BIS) value of 45-55. The cerebral oxygenation (rSO_2) values were taken from the bilateral forehead NIRS electrodes at baseline, at normocarbia and hypocarbia in both groups. The mean between the two groups and between normocarbia ($PaCO_2$ 36-38mmHg) and hypocarbia ($PaCO_2$ 30mmHg) was compared on the tumour and the normal side using unpaired t-test and repeated measures ANOVA test, respectively. A p-value of <0.05 was considered significant.

Both groups were similar with respect to demographic parameters. Hypocarbia caused a reduction in rSO_2 values in both groups, but it was statistically significant in Group P. When the rSO_2 values of the tumour side and normal side were analysed separately, there was a substantial decrease in the rSO_2 values in the P group from normocarbia to hypocarbia phase ($p<0.05$) on the normal side. There was no change in rSO_2 values on the tumour side.

Total intravenous anaesthesia (TIVA) with propofol can cause cerebral vasoconstriction, leading to ischemia in patients with raised ICP, especially during hyperventilation. Also, hyperventilation reduced cerebral oxygenation in patients with supratentorial tumours, which was more marked with TIVA. Close monitoring for cerebral desaturation is needed in neurosurgical patients when administering hyperventilation to reduce ICP, especially when using TIVA.

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APPENDICES

Technical Advisory Committee (Clinical Studies)

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
THIRUVANANTHAPURAM – 695011, INDIA

TAC Registration No: SCT-/S/2020/1081 **Date: 15.07.2020**

Project title: A COMPARISON OF THE EFFECT OF ANAESTHESIA WITH SEVOFLURANE AND PROPOFOL ON CEREBRAL OXYGENATION DURING HYPERVENTILATION IN PATIENTS UNDERGOING SUPRATENTORIAL TUMOUR EXCISION – A RANDOMISED CONTROL STUDY

Principal Investigator:
Dr Salini R Varma, Senior Resident, Division of Neuroanaesthesia and Neurocritical care, Department of Anaesthesiology, SCTIMST Degree: MBBS, MD
Co-Principal Investigator(s):
Dr Smita V, Associate Professor, Division of Neuroanaesthesia and Neurocritical care, Department of Anaesthesiology, SCTIMST Degree: MD, DM(Neuroanaesthesia)
Dr Unnikrishnan P, Assistant Professor, Division of Neuroanaesthesia and Neurocritical care, Department of Anaesthesiology, SCTIMST Degree: MD, PDCC(Neuroanaesthesia)

Members who participated in the TAC meeting on 20/06/2020

Dr Harikrishnan S (Chairman)
Dr Manikandan S
Dr Narayanan Namboodiri
Dr Jayadevan E R
Dr Sylaja P N
Dr Ramshekhar N Menon
Dr Unnikrishnan K P
Dr Syam K
Dr Sanjay G
Dr Deepti A N
Dr Sabarinath Menon
Dr Jayanand Sudhir B
Dr Srinivas G (Member Secretary)

Dr Sabarinath Menon, Dr Ramshekhar N Menon, Dr Sylaja P N, Dr Deepti A N, Dr Manikandan S, Dr Narayanan Namboodiri, Dr Srinivas G, Dr Sanjay G, Dr Harikrishnan S, Dr Unnikrishnan K P, Dr Syam K and Dr Jayadevan E R stayed away from the proceedings when the projects in which they are involved as investigator were discussed (#1072,1087, 1089, 1092, 1093, 1095, 1096, 1097, 1098, 1099, 1100, 1101, 1103, 1107, 1108, 1111, 1113, 1114, 1116, 1118, 1119, 1120, 1121, 1122, 1123, 1127, 1129, 1130)

Risk Classification of the project (Minimum/ Moderate/ High): Minimum
Requirement of DSMB: No
Recommended members of DSMB: Not applicable

Recommendations of TAC:
Recommended for consideration of IEC in the light of the responses received from the investigator

The PI may note that there can be no additions / alterations in the documents approved by TAC when they are submitted to the IEC.

Dr Srinivas G

MEMBER SECRETARY
TAC (Clinical Studies)
SCTIMST

Note for IEC
Copy of the investigator's responses to questions/suggestions from TAC is attached (Appendix-1).

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेंद्रम - 695 011, केरल, भारत
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY
TRIVANDRUM - 695 011, KERALA, INDIA
(एक राष्ट्रीय महत्व का संस्थान, विज्ञान एवं प्रौद्योगिकी विभाग, भारत सरकार)
(An Institution of National Importance, Department of Science and Technology, Government of India)
टेलीफॉन नं./Telephone No.: 0471-2443152 फैक्स/Fax: 0471-2446433, 2550728
ई-मेल/E-mail: sct@sctimst.ac.in वेबसाइट/Website: www.sctimst.ac.in

Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1565/OCTOBER-2020 30.10.2020

Dr. Salini R Varma
Senior Resident
Department of Anaesthesiology
SCTIMST, Thiruvananthapuram

Dear Dr. Salini R Varma,

Thank you for submitting documents related to your proposal titled "**A COMPARISON OF THE EFFECT OF ANAESTHESIA WITH SEVOFLURANE AND PROPOFOL ON CEREBRAL OXYGENNATION DURING HYPERVENTILATION IN PATIENTS UNDERGOING SUPRATENTORIAL TUMOUR EXCISION – A RANDOMIZED CONTROL STUDY'** (IEC/1565)" to the IEC for review.

The following documents were reviewed:

Original submission

1. *Check list*
2. *Covering letter addressed to Chairman dated 10.08.2020 endorsed by HoD*
3. *TAC Approval with Comments and responses*
4. *IEC Application dated 18/04/2020*
5. *Study Proposal*
6. *Proforma*
7. *Consent form(English)*
8. *Consent form(Malayalam)*
9. *Patient Information Sheet (English)*
10. *Patient Information Sheet (Malayalam)*
11. *Signed CV of PI ,Dr.Salini Varma, with TCMC Number*
12. *Signed CV of Co.PI Dr.Smita with TCMC Number*
13. *Signed CV of Co-PI Dr.Unnikrishnan with TCMC Number*

Revised submission on 06/10/2020

1. *Revised check list*
2. *Covering letter addressed to Chairman dated 10/8/2020 forwarded by HOD*
3. *TAC approval with comments and responses*
4. *IEC application form without required revisions*
5. *Study proposal*
6. *Proforma*
7. *Consent form in English*
8. *Consent form in Malayalam*
9. *Revised patient information sheet in English*
10. *Revised patient information sheet in Malayalam*
11. *Signed CV of PI ,Dr.Salini Varma, with TCMC Number*
12. *Signed CV of Co.PI Dr.Smita with TCMC Number*
13. *Signed CV of Co-PI Dr.Unnikrishnan with TCMC Number*

The following members of the Students Sub-Committee of the Institutional Ethics Committee participated in the discussions held between August 23-October 29,2020 at the offices and residences of the members

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
5.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
6.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
7.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

PATIENT INFORMATION SHEET

TITLE : "A comparison of the effect of anaesthesia with Sevoflurane and Propofol on cerebral oxygenation during hyperventilation in patients undergoing supratentorial tumour excision – a randomised controlled study."

Name of the Investigators: Dr.Salini R Varma (PI), Dr.Smita V (guide and CO-PI), Dr.Unnikrishnan P (Co guide and CO-PI)

You are being requested to participate in the above titled study which is being conducted to evaluate the usefulness of cerebral oxygenation monitoring sing Near Infrared Spectroscopy (NIRS) during hyperventilation given during surgery for supratentorial tumour excision with either sevoflurane or propofol as maintenance of anaesthesia. We have planned to recruit 50 people with supratentorial tumours posted for elective neurosurgical procedure at SCTIMST, Trivandrum. 25 patients will be given sevoflurane and 25 patients will be given propofol for maintenance of anaesthesia. You can belong to either one of the groups which will be decided randomly.

What is cerebral oxygenation monitoring by NIRS?

Our brain needs a constant supply of oxygen and nutrients for its proper functioning. There are various methods for assessing cerebral oxygenation of which NIRS is a non-invasive technology that continuously monitors regional tissue oxygenation. It is monitored by placing a pair of adhesive electrodes on each forehead of the participant.

What do you mean by anaesthesia with Sevoflurane/Propofol?

The agents for maintenance of anaesthesia keep you sedated throughout the surgical procedure. Anaesthesia can be maintained either by intravenous agents (e.g. Propofol) or by inhalational agents (e.g. Sevoflurane). Both are routinely being used in neurosurgical cases since long time without any significant side effects.

What is hyperventilation?

Hyperventilation is a technique which is given to reduce the arterial concentration of carbon dioxide. It is routinely being given during supratentorial tumour excision for improving the quality of surgical exposure and brain relaxation without any significant side effects.

If you take part what will you have to do?

Routine preanaesthetic check-up will be done on the day prior to the surgery. On the day of surgery, you will be taken inside the Neuro Operation Theatre. Non- invasive monitors to check your heart beat, blood pressure, oxygen saturation level and level of sedation (BIS electrode which is sticked on to your forehead) will be attached. An 18G intravenous cannula will be inserted under local anaesthesia in the hand for fluid and drug administration. The NIRS electrodes will be sticked on to each forehead and its baseline value will be noted.

Anaesthesia will be induced either by intravenous infusion or by inhalational route. After that you will be fully sedated and paralyzed, and you will be connected to ventilator. After that you will be hyperventilated as per standard practice and NIRS values will be noted down before and after hyperventilation, following which surgery is allowed to be continued.

Do NIRS, hyperventilation and maintenance of anaesthesia with sevoflurane or propofol have any side effects?

As NIRS is a non-invasive technique it does not carry any risk. Adverse events from doing this procedure is nil. Both intravenous agents like propofol and inhalational agents like sevoflurane are routinely being used in maintenance of anaesthesia in neurosurgical cases without any side effects. Hyperventilation is routinely given during supratentorial tumour surgeries for good surgical exposure and for brain relaxation.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any side effects, the study will be stopped and you will be given treatment for the side effects.

Will you have to pay for the cost of using the test?

These are used as a part of anaesthesia procedure for surgery. So no extra money will be charged for it.

Will your personal details be kept confidential?

The results of this study will be used for thesis submission as a part of academic research and will be submitted to a medical journal for publication, but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr. Salini R Varma (Principal investigator) mobile number: 9497324725. Email: salinirvarma@gmail.com

For technical advisory committee contact, please ask Dr. Mala Ramanathan, telephone number: 0471-2524234. Email: iec.mem.sec@sctimst.ac.in

രോഗിക്കുള്ള കാര്യവിവരണപത്രം

ശീർഷകം:

സൂപ്രാടെന്റോറിയൽ കലകളിലെ മുഴ നീക്കം ചെയ്യുന്നതിനുള്ള ശസ്ത്രക്രിയയ്ക്ക് വിധേയരാകുന്ന രോഗികൾക്ക് മസ്തിഷ്ക്കത്തിന്റെ ഒക്സിജനീകരണത്തിൽ സിവോഫ്ളൂറേനോ പ്രോപ്പോഫോളോ നൽകുമ്പോഴത്തെ ത്വരിത ശ്വസനത്തിലെ പ്രഭാവത്തിന്റെ താരതമ്യം - ക്രമാനുഗതമല്ലാതെ സന്നദ്ധപ്രവ്രർത്തകരിലെ ഒരു പഠനം.

ഗവേഷകരുടെ പേര്
ഡോ ശാലിനി ആർ വർമ്മ (പ്രധാന ഗവേഷക), ഡോ. സ്മിത വി (ഗൈഡും സഹഗവേഷകയും), ഡോ. ഉണ്ണികൃഷ്ണൻ പി (സഹഗൈഡും സഹഗവേഷകനും)

സൂപ്രാടെന്റോറിയൽ കലകളിലെ മുഴ നീക്കം ചെയ്യുന്നതിനുള്ള ശസ്ത്രക്രിയാ സമയത്ത് മയക്കം നിലനിർത്താനായി, സിവോഫ്ളൂറേനോടോ പ്രോപ്പോഫോളിനോടോ ഒപ്പം ത്വരിമായ ശ്വസനം നൽകുന്നതുകൊണ്ടുള്ള മസ്തിഷ്ക്കത്തിലെ ഓക്സജനീകരണം നിരീക്ഷിക്കുന്നതിൽ നീയർ ഇൻഫ്രാറെഡ് സ്പെട്രോസ്കോപ്പി (NIRS) യുടെ പ്രയോജനക്ഷമത വിലയിരുത്തുന്ന മുകളിൽ പറഞ്ഞ പഠനത്തിൽ പങ്കെടുക്കൻ താങ്കളോട് അഭ്യർത്ഥിക്കുന്നു. മുൻകൂർ നിശ്ചയിച്ച ന്യൂറോ ശസ്ത്രക്രിയയ്ക്ക് വിധേയരാകുന്ന സൂപ്രാടെന്റോറിയൽ മുഴയുള്ള രോഗികളിലെ 50 ആളുകളെ SCTIMST യിൽ നിന്നും തിരഞ്ഞെടുക്കൻ ഞങ്ങൾ ഉദ്ദേശിക്കുന്നു. മയക്കം നിലനിർത്താനായി 25 രോഗികൾക്ക സിവോഫ്ളൂറേനും 25 രോഗികൾക്ക് പ്രോപ്പോഫോളും നൽകും. താങ്കൾ ഉൾപ്പെടുന്നത്, ക്രമാനുഗതമല്ലാതെ തീരുമാനിക്കപ്പെടുന്ന സംഘങ്ങളിലേതെങ്കിലും ഒന്നിലായിരിക്കും.

മസ്തിഷ്ക്കത്തിലെ ഓക്സിജനീകരണത്തിന്റെ NIRS ഉപയോഗിച്ചുള്ള നിരീക്ഷണമെന്നാലെന്ത്?
നമ്മുടെ മസ്തിഷ്ക്കത്തിന്റെ ശരിയായ പ്രവർത്തനത്തിന് ഓക്സിജന്റെയും പോഷകങ്ങളുടെയും സ്ഥിരമായ ലഭ്യത അവശ്യമാണ്. മസ്തിഷ്ക്കത്തിലെ ഓക്സിജനീകരണം വിലയിരുത്തുന്നതിനുള്ള വ്യത്യസ്ത മാർഗ്ഗങ്ങളിൽ ഒന്നായ ശരീരത്തിൽ പ്രവേശിക്കാതെ പ്രാദേശികമായ കലകളുടെ ഓക്സജനീകരണം തുടർച്ചയായി നിരീക്ഷിക്കുന്ന സാങ്കേതികവിദ്യയാണിത്. പങ്കെടുക്കുന്ന ആളുടെ നെറ്റിയുടെ ഇരുവശത്തും ഒട്ടിച്ചുവയ്ക്കുന്ന ഇലക്ട്രോഡുകളിലൂടെയാണത് നിരീക്ഷിക്കുന്നത്.

സിവേഫ്ളൂറേൻ/പ്രൊപ്പോഫോൾ ഉപയോഗിച്ചുള്ള മയക്കെലെന്നതിന്റെ അർത്ഥമെന്ത്?
ശസ്ത്രക്രിയാ നടപടികളുടെ സമയം മുഴുവൻ താങ്കളുടെ മയക്കം നിലനിർത്തുന്നതിന് ഉപയോഗിക്കുന്ന മരുന്നുകളാണവ. കുത്തിവയ്ക്കുന്ന മരുന്നുകളിലൂടെയോ (ഉദാ. പൊപ്പൊഫോൾ) അല്ലെങ്കിൽ ശ്വസിപ്പിക്കുന്ന മരുന്നുകളിലൂടെയോ (ഉദാ. സിവോഫ്ളൂറേൻ) മയക്കം നിലനിർത്താൻ കഴിയും. ഇവ രണ്ടും പതിവായി ന്യൂറോശസ്ത്രക്രിയകളിൽ കാര്യമായ എന്തെങ്കിലും പാർശ്വഫലങ്ങളില്ലാതെ വളരെക്കാലമായി ഉപയോഗിച്ചു വരുന്നു.

ത്വരിത ശ്വസനമെന്നാലെന്ത്?
രക്തക്കുഴലുകളിൽ കാർബൺ ഡൈ ഓക്സൈഡിന്റെ കേന്ദ്രീകരണം കുറയ്ക്കാനായുള്ള ഒരു സങ്കേതമാണ് ത്വരിത ശ്വസനം. സൂപ്രടെന്റോറിയൽ കലകളിലെ മുഴ നീക്കം ചെയ്യുമ്പോൾ ശസ്ത്രക്രിയയുടെ ഗുണനിലവരവും മസ്തിഷ്ക്കത്തിന്റെ ആയാസരാഹിത്യവും മെച്ചപ്പെടുത്താൻ പതിവായി നൽകുന്ന കാര്യമായ പാർശ്വഫലങ്ങളില്ലാതെ ഒന്നാണത്.

താങ്കൾ പങ്കെടുക്കുന്നു എങ്കിൽ എന്തു ചെയ്യണം?
ശസ്ത്രക്രിയയുടെ തലേദിവസം മയക്കലിനുമുമ്പുള്ള പതിവ് പരിശോധനകൾ നടത്തും. ശസ്ത്രക്രിയാ ദിവസം താങ്കളെ ന്യൂറോശസ്ത്രക്രിയാ മുറിയിൽ പ്രവേശിപ്പിക്കും. താങ്കളുടെ

ഹൃദയമിടിപ്പ്, രക്തസമ്മർദ്ദം, പ്രാണവായുവിന്റെ പൂരിതാവസ്ഥയുടെ നിലവാരം, മയക്കത്തിന്റെ നിലവാരം (താങ്കളുടെ നെറ്റിയിൽ BIS ഇലക്ട്രോഡുകൾ ഘടിപ്പിക്കും) എന്നിവ ശരീരത്തിൽ പ്രവേശിക്കതെ നിരീക്ഷിക്കാനുള്ള ഉപകരണങ്ങൾ ഘടിപ്പിക്കും. ദ്രാവകങ്ങളും മരുന്നും നൽകുന്നതിനായി, പ്രാദേശിക മയക്കലിനു വിധേയമാക്കി ഒരു 18G വീനസ് കാനുല കൈയിൽ കടത്തും. ഇലക്ടോഡുകൾ നെറ്റിയുടെ ഇരുഭാഗത്തും ഒട്ടിച്ചു വെച്ച് അടിസ്ഥാന മൂല്യങ്ങൾ രേഖപ്പെടുത്തും.

കുത്തിവയ്പ്പിലൂടെയോ ശ്വസനത്തിലൂടെയോ മയക്കൽ തുടങ്ങും. താങ്കളെ പൂർണ്ണമായും മയക്കി സ്തംഭിപ്പിച്ച ശേഷം യാന്ത്രിക ശ്വസനസഹായിയുമായി ബന്ധിപ്പിക്കും.

അതിനുശഷം അംഗീകൃത പ്രവർത്തനത്തിന് അനുസൃതമായി താങ്കളെ ത്വരിത ശ്വസനത്തിന് വിധേയമാക്കുകയും ത്വരിത ശ്വസനത്തിനു മുമ്പും ശേഷവുമുള്ള മൂല്യങ്ങൾ രേഖപ്പെടുത്തുകയു ചെയ്യും.

എൻഐആർഎസ്സും (**NIRS**), സിവോഫ്ളൂറേനും പ്രൊപ്പോഫോളും ഉപയോഗിച്ച് മയക്കം നിലനിർത്തുന്നതും ത്വരിത ശ്വസനവും എന്തെങ്കിലും പാർശ്വഫലങ്ങളുണ്ടാക്കുമോ?

എൻഐആർഎസ്സ് ശരീരത്തിൽ പ്രവേശിക്കാതെയുള്ള സങ്കേതിക വിദ്യയായതിനാൽ അപായങ്ങളൊന്നുമില്ല. ഈ നടപടിയുടെ ഫലമായി പ്രതികൂല വിഷയങ്ങളൊന്നുമില്ല. കുത്തിവെയ്പ്പിലൂടെയുള്ള പ്രൊപ്പോഫോളും ശ്വസനത്തിലൂടെയുള്ള സിവോഫ്ളൂറേനും ന്യൂറോ ശസ്ത്രക്രിയയിൽ മയക്കം നിലനിർത്താൻ പതിവായി ഒരുതരത്തിലുള്ള പാർശ്വഫലങ്ങളുമില്ലാതെ ഉപയോഗിക്കുന്നു. സൂപ്രാടെന്റോറിയൽ കലകളിലെ മുഴ നീക്കം ചെയ്യുമ്പോൾ ശസ്ത്രക്രിയയുടെ ഗുണനിലവരവും മസ്തിഷ്ക്കത്തിന്റെ ആയാസരാഹിത്യവും മെച്ചപ്പെടുത്താനും പതിവായി നൽകുന്ന ഒന്നാണ് ത്വരിത ശ്വസനം.

പഠനം ആരംഭിച്ചശേഷം താങ്കൾക്ക് പിൻമാറാനാകുമോ?
ഈ പഠനത്തിലുള്ള താങ്കളുടെ പങ്കാളിത്തം പൂർണ്ണമായും സ്വമേധയായും പഠനത്തിലെ പങ്കാളിത്തം പിൻവലിക്കാൻ സ്വതന്ത്ര്യമുള്ളതുമാണ്. താങ്കളങ്ങനെ ചെയ്യുന്നതുകൊണ്ട് താങ്കളുടെ ചികിത്സയെ ഒരുവിധത്തിലും ബാധിക്കില്ല. അതിനൊപ്പം താങ്കൾക്കെന്തെങ്കിലും പാർശ്വഫലമുണ്ടായാൽ പഠനം നിർത്തുകയും പാർശ്വഫലത്തിന് ചികിത്സ നൽകുകയും ചെയ്യും.

പരിശോധനയുടെ ചിലവിനുള്ള പണം താങ്കൾ നൽകണോ?
ഇവ ഉപയോഗിക്കുന്നത് മയക്കൽ പ്രക്രിയയുടെ ഭാഗമായാണ്. ആകയാൽ അധികം പണം ഈടാക്കില്ല.

താങ്കളുടെ വ്യക്തി വിവരങ്ങൾ രഹസ്യമായിരിക്കുമോ?
അക്കാഡമിക് ഗവേഷണത്തിന്റെ ഭാഗമായ തീസീസ് സമർപ്പിക്കലിന് ഈ പഠനത്തിന്റെ ഫലങ്ങൾ ഉപയോഗിക്കുകയും ഒരു വൈദ്യശാസ്ത്ര ജേർണലിൽ പ്രസിദ്ധീകരിക്കുകയും ചെയ്യും, പക്ഷേ പ്രസിദ്ധീകരണത്തിലോ പ്രദർശനത്തിലോ താങ്കളെ പേരുകൊണ്ട് തിരിച്ചറിയാനാകില്ല. എന്നിരുന്നാലും, താങ്കൾ പഠനത്തിൽ പങ്കെടുക്കുകയാണെങ്കിൽ, താങ്കളുടെ വൈദ്യചികിത്സാ രേഖകൾ ഈ പഠനവുമായി ബന്ധപ്പെട്ടവർ താങ്കളുടെ വീണ്ടുമുള്ള അനുവാദമില്ലാതെ വിലയിരുത്തിയേക്കാം.

താങ്കൾക്ക് കൂടുതലെന്തെങ്കിലും ചോദ്യങ്ങളുണ്ടെങ്കിൽ ദയവായി ഡോ ശാലിനി ആർ വർമ്മയോട് ചോദിക്കുക. മൊബൈൽ നമ്പർ 9497324725. ഇമെയിൽ. salinirvarma@gmail.com

നൈതീക അനുവാദവുമായി ബന്ധപ്പെട്ട ചോദ്യങ്ങൾക്ക് ഡോ. മാലാ രാമനാഥനനെ ബന്ധപ്പെടുക മൊബൈൽ നമ്പർ 0471-2524234. ഇമെയിൽ. iec.mem.sec@sctimst.ac.in

CONSENT FORM

STUDY TITLE: A comparison of the effect of anaesthesia with Sevoflurane and Propofol on cerebral oxygenation during hyperventilation in patients undergoing supratentorial tumour excision – a randomised controlled study

Participant's name: Age (in years):

I_____, son/daughter of _____

Declare that (Please tick boxes)

• I have read the above information provided to me regarding the study "A comparison of the effect of anaesthesia with Sevoflurane and Propofol on cerebral oxygenation during hyperventilation in patients undergoing supratentorial tumour excision – a randomised controlled study." [ ]

• I have clarified any doubts that I had. [ ]

• I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]

• I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]

• I understand that my identity will not be revealed in any information released to third parties or published [ ]

• I voluntarily agree to take part in this study [ ]

• I have been provided with the contact numbers of the principle investigator, in case I want to know more about the study and participants rights [ ].

• I received a copy of this signed consent form [ ]

Name:

Signature:

Date:

Name of witness:

Relation to participant:

Signature:

Person Obtaining Consent

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

Name:

Signature: Date:

സമ്മതപത്രം

ശീർഷകം:

സൂപ്രാടെന്റോറിയൽ കലകളിലെ മുഴ നീക്കം ചെയ്യുന്നതിനുള്ള ശസ്ത്രക്രിയയ്ക്ക് വിധേയരാകുന്ന രോഗികൾക്ക് മസ്തിഷ്ക്കത്തിന്റെ ഒക്സിജനീകരണത്തിൽ സിവോഫ്ളൂറേനോ പ്രോപ്പോഫോളോ നൽകുമ്പോഴത്തെ ത്വരിത ശ്വസനത്തിലെ പ്രഭാവത്തിന്റെ താരതമ്യം - സന്നദ്ധപ്രവ്രാത്തകരിലെ ക്രമാനുഗതമല്ലാതെ ഒരു പഠനം

പങ്കെടുക്കുന്നയാളുടെ പേര്_____ വയസ് (വർഷത്തിൽ) __

ഞാൻ _____മകൻ/മകൾ_____

പ്രഖ്യാപിക്കുന്നതെന്തെന്നാൽ (ദയവായി കളങ്ങളിൽ ശരിയടയാളമിടുക)

- 'സൂപ്രാടെന്റോറിയൽ കലകളിലെ മുഴ നീക്കം ചെയ്യുന്നതിനുള്ള ശസ്ത്രക്രിയയ്ക്ക് വിധേയരാകുന്ന രോഗികൾക്ക് മസ്തിഷ്ക്കത്തിന്റെ ഒക്സിജനീകരണത്തിൽ സിവോഫ്ളൂറേനോ പ്രോപ്പോഫോളോ നൽകുമ്പോഴത്തെ ത്വരിത ശ്വസനത്തിലെ പ്രഭാവത്തിന്റെ താരതമ്യം - സന്നദ്ധപ്രവ്രാത്തകരിലെ ക്രമാനുഗതമല്ലാതെ ഒരു പഠനം' സംബന്ധമായി മുകളിൽ നൽകിയ വിവരങ്ങൾ വായിച്ചു. [ ]
- എനിക്കുണ്ടായ സംശയങ്ങൾ പരിഹരിച്ചു. [ ]
- എന്റെ പങ്കാളിത്തം സ്വമേധയായാണെന്നും, എന്റെ പതിവ് ചികിത്സയെയോ നിയമപരമായ അവകാശങ്ങളോയോ ബാധിക്കാതെ ഏതു സമയത്തും പങ്കെടുക്കുനനതിനുള്ള എന്റെ അനുവാദം പിൻവലിക്കാമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- ഞാൻ പഠനത്തിൽ നിന്നും പിൻമാറിയാലും എന്റെ ചികിത്സാരേഖകൾ പരിശോധിക്കാൻ
- പഠന സംഘാംഗങ്ങൾക്കോ ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്സ് കമ്മിറ്റി അംഗങ്ങൾക്കോ എന്റെ അനുവാദം ആവശ്യമില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു, അതിന് ഞാൻ സമ്മതിക്കുന്നു. [ ]
- മൂന്നാം കക്ഷികൾക്കു നൽകുമ്പോഴും പ്രസിദ്ധീകരിക്കുമ്പോഴും എന്റെ വ്യക്തിവിവരങ്ങൾ നൽകില്ലെന്ന് മനസ്സിലാക്കുന്നു. [ ]
- ഞാൻ സ്വമേധയാ ഈ പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിക്കുന്നു. [ ]
- പഠനത്തെപ്പറ്റിയോ പങ്കെടുക്കുന്നവരുടെ അവകാശങ്ങളെപ്പറ്റിയോ കൂടുതലറിയണമെങ്കിൽ ബന്ധപ്പെടാൻ പ്രധാന ഗവേഷകയുടെ ബന്ധപ്പെടാനുള്ള നമ്പറുകൾ എനിക്ക് ലഭിച്ചിട്ടുണ്ട്. [ ]
- സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് ലഭിച്ചു. [ ]

പേര്

ഒപ്പ്

തീയതി

സാക്ഷിയുടെ പേര്

രോഗിയുമായുള്ള ബന്ധം

ഒപ്പ്

സമ്മതപത്രം വാങ്ങുന്ന ആൾ

മെഡിക്കൽ റിസർച്ച്പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണ പദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകടസാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതപത്രംവാങ്ങുന്ന ആളുടെ പേര്

ഒപ്പ് തീയതി

PROFORMA

STUDY TITLE: "A comparison of the effect of anaesthesia with Sevoflurane and Propofol on cerebral oxygenation during hyperventilation in patients undergoing supratentorial tumour excision – A randomised controlled study."

Serial no.
Date:

Age:	
Sex:	
Diagnosis:	
Preoperative complaints:	
Preoperative MRI:	
ASA Grade	
GCS	
Signs of raised intracranial pressure: (Clinical/Radiological signs)	Yes / No Midline shift:
History of stroke/Transient ischemic attacks/ carotid artery disease:	Yes / No
Uncontrolled diabetes mellitus/systemic hypertension/cardiovascular disease/COPD:	Yes / No
Anaesthetic agents used:	Group S / Group P

CEREBRAL OXYGENATION (NIRS)

	Right	Left	Average
Before induction			
FiO_2 0.5			
Normocarbia ($PaCO_2$ 36-38mmHg)			
Hypocarbia ($PaCO_2$ 30mmHg)			

Haemodynamic parameters

	Heart rate	MAP	SPO_2	Number of boluses of Mephentermine
Baseline (Before induction)				
Normocarbia ($PaCO_2$ 36-38mmHg)				
Hypocarbia ($PaCO_2$ 30mmHg)				

Anaesthetic concentration

	MAC (Group S)	Effect site concentration (Group P)	BIS Value
Before induction			
Normocarbia ($PaCO_2$ 36-38mmHg)			
Hypocarbia ($PaCO_2$ 30mmHg)			

Ventilatory parameters

	FiO_2	PaO_2	$EtCO_2$	$PaCO_2$	Minute ventilation
Before induction					
Normocarbia ($PaCO_2$ 36-38mmHg)					
Hypocarbia ($PaCO_2$ 30mmHg)					

Name and signature of the investigator (with date):

Sl no	Age	Sex	Diagnosis	ASA class	Preop com	Tumour volume	MLS	GCS	Signs of ra	DM/HTN	TIA/Caroti	Group P/S	NIRS												
													Tumour side				Normal side				AVERAGE				
													Before ind	FiO2 0.5	Normocarb	Hypocarbia	Before ind	FiO2 0.5	Normocarb	Hypocarbia	Before ind	FiO2 0.5	Normocarb	Hypocarbia	Heart rate
1	18	M	Left frontal anaplastic ol	1	headache,s	27.9	3	15	N	N	N	P	70	71	68	64	70	71	66	57	70	71	67	60.5	68
2	25	F	Left frontal glioma	1	headache,b	18.48	4	15	N	N	N	P	73	75	68	62	70	72	64	57	71.5	73.5	66	59.5	58
3	55	F	Left sphenoid wing men	1	headache,r	173.4	7	15	N	N	N	P	71	71	69	66	68	68	66	63	69.5	69.5	67.5	64.5	68
4	56	M	Left frontal convexity m	2	headache,s	47.48	3	15	N	N	N	P	73	73	66	64	69	69	63	59	71	71	64.5	61.5	73
5	33	M	Left frontal glioma	1	seizure	103.54	8	15	N	N	N	S	69	71	70	69	65	67	69	68	67	69	69.5	68.5	67
6	58	M	Left frontal glioma	2	seuzure,he	12	3	15	N	N	N	P	64	67	68	64	65	66	61	64	64.5	67	67	62.5	68
7	60	F	Left frontal glioma	2	seuzure,he	27.77	5	15	N	N	N	S	71	72	70	70	70	71	69	70	70.5	71.5	69.5	70	82
8	45	M	Left temporal high grade	1	seuzure,he	82.5	4	15	N	N	N	P	70	71	69	65	72	74	73	69	71	72.5	71	67	63
9	34	F	Right parietal glioma	2	seuzure,he	45.57	6	15	N	N	N	P	67	67	64	59	74	74	66	61	70.5	70.5	65	60	61
10	29	F	Right frontal glioma	1	seizure	105	8	15	N	N	N	S	64	65	69	64	61	63	67	60	62.5	64	68	62	58
11	43	M	Right frontal glioma	1	seizure	72	3	15	N	N	N	S	66	69	70	69	62	64	68	65	64	66.5	69	67	58
12	27	M	Left parietal glioma	1	seizure,me	27.93	4	15	N	N	N	P	71	71	70	70	62	62	58	55	66.5	66.5	64	57.5	82
13	57	M	Left frontal lymphoma	2	seizure,NH	17.16	7	15	N	N	N	S	64	64	67	58	64	64	63	55	64	64	65	56.5	70
14	60	M	Left parietal glioma	2	seizure	10.39	4	15	N	N	N	S	69	69	66	64	72	72	68	64	70.5	70.5	67	64	68
15	54	F	Left frontal glioma	2	seizure	2.13	4	15	N	N	N	S	62	62	63	63	58	58	61	52	60	60	62	57.5	80
16	34	M	left insular glioma	1	seizure	162	4	15	N	N	N	P	71	71	68	65	75	75	70	68	73	73	69	66.5	62
17	38	M	Left frontal glioma	1	seizure	19.11	4	15	N	N	N	P	72	72	68	65	72	73	66	59	72	72.5	67	62	70
18	48	M	Right temporal glioma	2	seuzure,he	48.74	6	15	N	N	N	S	72	72	70	70	73	73	71	70	72.5	72.5	70.5	70	58
19	36	M	Left frontal glioma	1	seizure,syn	57.76	5	15	N	N	N	P	72	72	70	66	70	70	66	62	71.5	71.5	68	64	82
20	28	M	Left frontal glioma	1	seuzure,he	3.55	6.2	15	N	N	N	S	64	65	65	64	63	64	65	64	63.5	64.5	65	64	69
21	41	M	Right temporal glioma	1	seizure	117.6	5.4	15	N	N	N	S	68	68	65	63	70	70	65	61	69	69	65	62	78
22	40	M	Right frontal glioma	2	seizure	3.15	3.5	15	N	N	N	P	65	67	70	71	67	69	71	65	66	68	70.5	68	72
23	24	M	Right frontal glioma	1	seizure	8.25	0	15	N	N	N	P	69	69	64	58	72	72	65	64	70.5	70.5	60.5	64	68
24	39	M	Right frontal glioma	1	seuzure,he	21.38	0	15	N	N	N	P	70	70	64	59	72	72	66	65	71	71	65	63	68
25	58	F	Right frontal glioma	1	seuzure,he	93.33	5.2	15	N	N	N	P	70	70	71	68	68	68	70	64	69	69	70.5	66	72
26	51	F	Right temporal glioma	2	seizure	4.4	3	15	N	N	N	S	71	71	70	68	68	68	67	64	69.5	69.5	68.5	66	68
27	41	M	Right perisylvian glioma	1	seuzure,he	84	5.2	15	N	N	N	S	70	70	67	65	71	71	68	65	70.5	70.5	67.5	65	56
28	34	M	Right temporal glioma	1	seizure	145.64	6	15	N	N	N	S	69	70	65	62	72	73	64	60	70.5	71.5	64.5	61	70
29	60	M	Left frontal glioma	1	seuzure,he	74.15	7	15	N	N	N	P	64	64	57	55	62	62	54	53	63	63	55.5	54	88
30	59	M	Left parietal glioma	2	headache,F	21.6	6.2	15	N	N	N	S	68	69	68	67	68	69	67	65	68	69	67.5	66	71
31	56	F	Left frontal oligodendrog	1	headache,s	18.2	3	15	N	N	N	P	70	71	66	58	68	69	64	52	69	70	65	55	60
32	55	F	Left frontal glioma	1	seuzure,he	35.72	7	15	N	N	N	S	62	65	68	66	59	62	62	59	60.5	63.5	65	62.5	72
33	51	F	Left frontal glioma	1	headache,r	45.2	8.4	15	N	N	N	P	72	72	68	64	70	70	66	57	71	71	67	60.5	58
34	50	F	Right frontal glioma	2	seuzure,he	47.04	6	15	N	N	N	S	68	68	66	65	64	64	63	62	66	66	64.5	63.5	76
35	49	F	Right frontal glioma	1	seuzure,he	27.2	5	15	N	N	N	S	66	66	65	64	70	70	69	68	68	68	67	66	71
36	44	M	Right frontal glioma	2	seizure	92.63	7	15	N	N	N	S	70	71	65	64	73	73	68	67	71.5	72	66.5	65.5	78
37	32	M	Right frontal glioma	1	seizure	18.25	3.5	15	N	N	N	P	64	66	60	57	66	68	64	60	65	67	62	58.5	58
38	52	F	Left frontal glioma	1	seuzure,he	98	7	15	N	N	N	P	70	73	72	68	60	63	61	65	65	68	66.5	62	65
39	60	M	Right frontal glioma	2	seuzure,he	20.58	5.6	15	N	N	N	S	67	69	65	65	66	67	65	64	66.5	68	65	64.5	71
40	57	M	Right parietal glioma	1	seizure,me	99.1	5.2	15	N	N	N	P	68	68	64	59	72	72	66	62	70	70	65	60.5	70
41	35	M	Right frontal glioma	2	seuzure,he	41.2	6	15	N	N	N	P	69	71	72	69	71	74	72	69	70	72.5	72	69	70
42	53	M	Right frontal glioma	1	seuzure,he	21	3	15	N	N	N	S	70	70	69	64	66	66	65	63	68	68	67	63.5	55
43	58	F	Left frontal glioma	1	Memory di	40.4	6	15	N	N	N	S	70	72	65	64	69	70	64	62	69.5	71	64.5	63	82
44	42	M	Right frontotemporal gli	2	seizure	35	5	15	N	N	N	P	68	71	68	65	72	75	70	68	70	73	69	66.5	68
45	60	M	Right frontal glioma	2	seuzure,he	74.52	5	15	N	N	N	S	72	74	70	69	73	74	70	68	72.5	74	70	68.5	57
46	23	M	Right frontal glioma	1	seizure	39.9	5.1	15	N	N	N	S	72	73	69	67	73	76	69	68	72.5	74.5	69	67.5	72
47	32	M	Left frontal glioma	1	seuzure,he	19.6	4.7	15	N	N	N	S	73	74	70	69	74	74	70	68	73.5	74	70	68.5	80
48	30	F	Right frontal glioma	1	seuzure,he	35.16	5.3	15	N	N	N	P	60	62	65	69	62	63	67	58	61	62.5	66	63.5	52
49	33	M	Left frontal glioma	2	seuzure,he	18.3	3	15	N	N	N	S	67	70	71	68	68	70	72	68	67.5	70	71.5	68	74
50	27	M	Left frontal glioma	1	seuzure,he	17.7	4	15	N	N	N	P	68	69	67	65	67	68	66	60	67.5	68.5	66.5	62.5	80

Haemodynamic parameters										
Before induction			At normocarbia				Hypocarbia			
BP	SpO2	No of bolu	Heart rate	SpO2	BP	No of bolu	Heart rate	SpO2	BP	No of bolu
100	100	0	72	100	71	0	70	100	69	0
93	100	0	62	100	77	0	60	100	73	0
77	100	0	67	100	93	1	64	100	87	0
78	100	0	70	100	82	1	70	100	86	0
73	100	0	68	100	75	1	65	100	73	0
92	100	0	72	100	91	0	70	100	73	0
105	100	0	76	100	74	1	77	100	87	1
93	100	0	59	100	94	1	61	100	93	0
86	100	0	64	100	88	1	62	100	84	0
93	100	0	62	100	77	0	60	100	73	0
77	100	0	62	100	82	1	60	100	73	0
93	100	0	78	100	77	1	76	100	73	0
75	100	0	68	100	75	1	64	100	76	1
72	100	0	72	100	74	1	71	100	76	0
81	100	0	84	100	80	0	76	100	82	0
93	100	0	58	100	77	0	57	100	73	0
71	100	0	74	100	78	1	71	100	73	0
74	100	0	55	100	75	1	56	100	76	0
77	100	0	80	100	82	0	84	100	73	1
90	100	0	67	100	78	1	64	100	78	0
81	100	0	76	100	75	0	70	100	82	1
76	100	0	70	100	72	0	69	100	73	0
95	100	0	64	100	86	0	60	100	90	0
76	100	0	59	100	72	1	61	100	73	0
93	100	0	66	100	90	0	68	100	91	0
81	100	0	72	100	83	1	70	100	82	1
74	100	0	54	100	80	1	50	100	74	0
81	100	0	65	100	80	1	62	100	82	0
90	100	0	80	100	82	1	78	100	84	0
72	100	0	70	100	74	2	72	100	76	0
67	100	0	62	100	68	1	65	100	68	0
77	100	0	74	100	93	0	70	100	87	1
80	100	0	54	100	84	0	53	100	73	1
71	100	0	68	100	76	1	69	100	79	0
92	100	0	68	100	92	1	65	100	92	0
93	100	0	72	100	75	1	71	100	90	0
74	100	0	51	100	72	0	52	100	73	0
90	100	0	61	100	86	1	67	100	87	0
84	100	0	80	100	83	0	78	100	87	0
75	100	0	68	100	75	1	64	100	76	1
81	100	0	76	100	75	1	72	100	81	0
80	100	0	58	100	81	1	58	100	79	0
92	100	0	80	100	87	0	81	100	88	0
93	100	0	62	100	77	1	64	100	80	0
93	100	0	60	100	89	0	61	100	88	0
91	100	0	70	100	85	0	69	100	87	0
81	100	0	82	100	80	0	80	100	82	0
78	100	1	53	100	76	0	54	100	74	0
74	100	0	70	100	80	1	68	100	74	0
87	100	0	82	100	86	1	79	100	83	0

Anaesthetic concentration									
MAC(Group S)			Effect site concentration(Group P)			BIS value/ Psi value			
before indu	Normocarb	Hypocarbia	before indu	Normocarb	Hypocarbia	before indu	Normocarb	Hypocarbia	
				4	3	100	46	45	
				3	2.5	100	49	46	
				3	2.5	100	50	49	
				4	2.5	100	47	48	
	1	1.2				100	45	46	
				4.1	3.7	100	48	47	
				4	2.5	100	48	47	
				3.5	3	100	50	49	
				3.5	3	100	47	48	
	1.2	1.1				100	46	45	
	1.1	1				100	47	45	
				4	3	100	47	47	
	1.3	1.1				100	46	45	
	1.2	1.1				100	50	49	
	1.2	1				100	50	52	
				3.5	2.5	100	46	47	
				3.5	2.8	100	45	46	
	1.2	0.9				100	47	47	
				4	3	100	46	47	
	0.9	0.9				100	48	48	
	1.1	0.9				100	50	52	
				3.3	3.1	100	53	54	
				3.5	3	100	49	48	
				3.5	3	100	45	46	
				3.5	3	100	48	46	
	1	0.8				100	46	45	
	1.2	1				100	45	46	
	0.9	0.9				100	46	47	
				4	2.5	100	46	47	
	1.1	0.9				100	47	46	
				4	2.5	100	46	45	
	1.3	1.1				100	49	48	
				3	2.5	100	48	47	
	1.1	0.9				100	47	45	
	1	0.9				100	47	45	
	1	0.9				100	48	47	
				3	2.8	100	50	48	
				4	3.8	100	46	45	
	1.1	1				100	47	46	
				3.8	3.1	100	48	47	
				3.1	2.5	100	53	51	
	0.9	0.9				100	50	48	
	1.1	1				100	47	45	
				3.5	2.5	100	48	47	
	1.1	1				100	49	48	
	1.3	1.1				100	48	46	
	1.2	1				100	45	46	
				3.5	3	100	47	48	
	1.1	0.9				100	49	47	
				4	3.5	100	48	46	

Ventilatory parameters										
Normocarbia					Hypocarbia					
FiO2	PaO2	EtCO2	PaCO2	Minute ver	FiO2	PaO2	EtCO2	PaCO2	minte ventilation	
0.5	268	31	36	5.4	0.5	260	26	31	8	
0.5	220	32	38	5.28	0.5	242	24	29	7.5	
0.5	240	32	37	6	0.5	236	25	31	7.2	
0.5	291	30	37	6	0.5	289	23	30	7.2	
0.5	245	33	37.1	5.6	0.5	250	27	29.9	7.4	
0.5	232	32	36.8	5.6	0.5	228	27	31.1	7.2	
0.5	258	33	37	5.8	0.5	312	25	29	8.2	
0.5	226	32	39	5.7	0.5	212	24	31	7.3	
0.5	265	33	36	5.6	0.5	256	27	29	7	
0.5	252	33	37.2	5.4	0.5	239	25	29.8	6.8	
0.5	224	32	38	5.8	0.5	216	26	30.1	7.2	
0.5	230	32	36.1	5.2	0.5	235	27	30.5	6.6	
0.5	200	30	36.5	6	0.5	198	24	29.6	8.1	
0.5	212	31	38.2	5.5	0.5	197	26	31.1	6.8	
0.5	221	32	36.1	5.6	0.5	220	26	30.3	6.9	
0.5	210	33	36	5.2	0.5	205	26	30	7.2	
0.5	228	31	37	5.6	0.5	220	24	29	7.2	
0.5	252	33	36	5.6	0.5	246	27	31	7.2	
0.5	231	32	37	5.6	0.5	222	25	31	8	
0.5	250	34	37	5.8	0.5	243	28	31	8	
0.5	268	31	37	6	0.5	259	25	31	8	
0.5	149	34	38	6.4	0.5	140	26	31	7.4	
0.5	240	32	37	5.7	0.5	235	26	29	7.1	
0.5	289	32	39	6	0.5	285	25	31	8	
0.5	243	34	38	5.2	0.5	239	26	31.2	7.2	
0.5	238	31	37	7.2	0.5	237	24	30	8	
0.5	253	31	36.8	6	0.5	249	25	30.7	8	
0.5	230	33	38	7.2	0.5	232	26	30	8	
0.5	228	33	39	5.7	0.5	224	27	32	7.8	
0.5	256	30	38	8	0.5	246	21	30	10	
0.5	143	32	39	7.8	0.5	135	23	30	8.2	
0.5	196	30	36	5.2	0.5	189	25	30.2	6.1	
0.5	221	33	36	5.6	0.5	223	25	29	6.9	
0.5	263	33	39	6	0.5	258	26	31	7.2	
0.5	259	31	36	5.6	0.5	263	24	29	7.2	
0.5	228	32	38	5.7	0.5	232	25	31	7.3	
0.5	230	32	36	7.2	0.5	220	26	29	8	
0.5	243	31	35.9	5.6	0.5	238	26	30.2	6.9	
0.5	265	29	37	6	0.5	256	22	30	7.2	
0.5	238	33	39	5.8	0.5	222	25	30	8.2	
0.5	252	34	38.3	5.8	0.5	241	28	31	7.2	
0.5	248	32	36.8	7.2	0.5	250	24	31	8	
0.5	270	32	39	5.6	0.5	265	24	30	7.2	
0.5	222	33	38	5.7	0.5	218	24	30.8	7.8	
0.5	235	31	37.2	5.8	0.5	219	26	30.2	7.9	
0.5	245	29	36.8	5.9	0.5	238	23	29.8	7.3	
0.5	248	31	38	5.6	0.5	239	25	31	6.8	
0.5	145	35	37	6	0.5	147	28	29	7.2	
0.5	238	32	37	6.4	0.5	229	25	30.1	7.6	
0.5	242	31	38.7	5.9	0.5	240	24	29.2	7.9	

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