COMPARISON OF THE EFFECT OF PROPOFOL Vs DEXMEDETOMIDINE INFUSION ON UNMASKING THE FOCAL NEUROLOGICAL DEFICITS AND SOMATOSENSORY EVOKED POTENTIAL (SSEP) CHANGES IN SUPRATENTORIAL BRAIN TUMORPATIENTS UNDERGOING NEUROSURGERY.

Dr. Sapna Suresh

DM THESIS

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SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES

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A THESIS SUBMITTED BY

DR SAPNA SURESH

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM.

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE AWARD OF

DM NEUROANESTHESIA

YEAR 2022

DECLARATION BY THE STUDENT

CERTIFICATE

I, Sapna Suresh, hereby declare that I have personally carried out the work depicted in thesis titled **'Comparison of the effect of Propofol vs Dexmedetomidine infusion on unmasking the focal neurological deficits and somatosensory evoked Potential (SSEP) changes in supratentorial brain tumor patients undergoing neurosurgery'.**

No part of this thesis has been submitted for award of any other degree or diploma prior to the date.

Date: 27/07/2022

Place: Thiruvananthapuram

Dr. Sapna Suresh,

DM Neuroanesthesia Resident,

Division of Neuroanaesthesia and Neurocriticalcare

Department of Anaesthesiology,

SCTIMST, Thiruvananthapuram

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेंद्रम , केरल– 695 011
(एक राष्ट्रीय महत्व का संस्थान, विज्ञान एवं प्रौद्योगिकी विभाग, भारत सरकार)
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
KERALA – 695 011
(An Institution of National Importance, Department of Science and Technology, Govt. of India)
टेलीफॉन नं.Telephone No. 2443152-0471फाक्स/Fax2446433,2550728-0471
ई-मेल/E-mail :sct@sctimst.ac.in वेबसाइट/ Website : www.sctimst.ac.in

CERTIFICATE BY THE RESEARCH GUIDE

Name of the Guide: DR Manikandan.S

Division of Neuroanesthesia and Neurocritical care.

This is to certify that Sapna Suresh, division of Neuroanesthesia and Neurocritical care of this institute has fulfilled the requirements prescribed for the DM degree of the Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum .

The thesis entitled, "Comparison of effect of Propofol vs Dexmedetomidine infusion on unmasking the focal neurological deficits and somatosensory evoked potential (SSEP) changes in supratentorial brain tumour patients undergoing neurosurgery" was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date.

*Clearance was obtained from the Institutional Ethics Committee and CTRI for carrying out the study.

Signature

Name of the Guide
PROF(DR)MANIKANDAN.S,M.D.PDCC

Date 22/07/2022

Dr. S. MANIKANDAN MD, PDCC
Professor and In-charge
Division of Neuroanaesthesia &
Neurocritical Care
Sree Chitra Tirunal Institute for
Medical Sciences and Technology
Thiruvananthapuram - 695 011

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेंद्रम , केरल– 695 011
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SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
KERALA – 695 011
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टेलीफॉन नं.Telephone No. 2443152-0471फाक्स/Fax2446433,2550728-0471
ई-मेल/E-mail :sct@sctimst.ac.in वेबसाइट/ Website : www.sctimst.ac.in

CERTIFICATE BY THE RESEARCH CO-GUIDE

Name of the Guide: DR Unnikrishnan .P

Division of Neuroanesthesia and Neurocritical care

This is to certify that Sapna Suresh, division of this institute has fulfilled the requirements prescribed for the DM degree of the Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum.

The -work under the thesis entitled, "Comparison of the effect of propofol vs dexmedetomidine infusion on unmasking the focal neurological deficits and somatosensory evoked potential (SSEP) changes in supratentorial brain tumour patients undergoing neurosurgery" was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date.

*Clearance was obtained from the Institutional Ethics Committee Research and CTRI committees for carrying out the study.

Name of the Co-guide
DR Unnikrishnan .P M.D,PDCC

Date:27/07/2022

Thiruvananthapuram

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेंद्रम , केरल– 695 011
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ई-मेल/E-mail :sct@sctimst.ac.in वेबसाइट/ Website : www.sctimst.ac.in

CERTIFICATE

This is to certify that this thesis entitled "Comparison of effect of Propofol versus Dexmedetomidine infusion on unmasking the focal neurological deficits and somatosensory evoked potential (SSEP) changes in supratentorial brain tumour patients undergoing neurosurgery" is a bonafide work of Dr Sapna Suresh, Division of Neuroanesthesia and Neurocritical Care of this institute . This work was done under the keen supervision of her guide, Dr Manikandan S, and she has shown keen interest and hard work in this thesis.

29-7-2022

Date:29-7-2022

Thiruvananthapuram

Dr Shrinivas V.G
Senior Professor and Head
Department of Anesthesiology, SCTIMST

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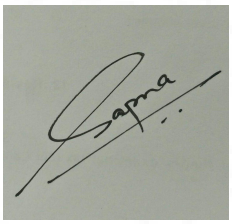
Words prove a meagre media to write down my feelings for my mother in law Dr Geetha Prabhu who stepped up during my time of need and was a mother figure to my daughter Trishika .



Date **: 26/07/2022**

Dr Sapna Suresh

Senior Resident

Thiruvananthapuram

DM Neuroanesthesia

SCTIMST

CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

ACNS	**:**	American Clinical Neurophysiology Society
ASA	**:**	American society of Anesthesiologists
ANOVA	**:**	Analysis of Variance
BIS	**:**	Bi spectral Index
BOLD	**:**	Blood Oxygen level Dependent Signal
Bpm	**:**	Beats per minute
CBF	**:**	Cerebral Blood Flow
CNS	**:**	Central nervous system
CVS	**:**	Cardiovascular system
COPD	**:**	Chronic Obstructive Pulmonary Disease
CTRI	**:**	Clinical Trials Registry of India
DES.	**:**	Direct Electric Stimulation
DTI	**:**	Diffuse Tensor Imaging
EEG	**:**	Electroencephalography
ETCO2	**:**	End tidal CO2
fMRI	**:**	Functional MRI
GABA	**:**	Gamma Amino Butyric Acid
GBM	**:**	Glioblastoma Multiforme
GCS	**:**	Glasgow Coma Scale
HCl	**:**	Hydrochloric acid
HR	**:**	Heart rate
Hz	**:**	Hertz
ICU	**:**	Intensive care Unit
mA	**:**	milliampere
µg/kg	**:**	microgram /kilogram
µg/kg/hr	**:**	microgram/kg/hour
µg/ml	**:**	microgram / milliliter
MEG	**:**	Magnetoencephalography
ml/kg	**:**	milliliter/kilogram

MRI	**:**	Magnetic Resonance Imaging
NIBP	**:**	Noninvasive blood pressure
NIHSS	**:**	National Institute of Health Stroke Scale
NPO	**:**	Nil per oral
NSOT	**:**	Neurosurgical operating theatres
OAA/S	**:**	Observer Assessment of Alertness/Sedation scale
PHT	**:**	Peg Hole Test
pka	**:**	acid dissociation constant
PONV	**:**	Post operative nausea and vomiting
PTN	**:**	Posterior tibial nerve
REZ	**:**	Root entry zone
RS	**:**	Respiratory system
SCTIMST	**:**	Sree Chitra Tirunal institute of Medical Sciences
SSEP	**:**	Somatosensory evoked potential
SPO_2	:	Arterial Oxygen Saturation
TCI	**:**	Target controlled infusion
VPL	**:**	Ventroposterolateral nucleus of thalamus
WHO	**:**	World Health Organization

ABSTRACT

Title:

"COMPARISION OF EFFECT OF PROPOFOL Vs DEXMEDETOMIDINE INFUSION ON UNMASKING THE FOCAL NEUROLOGICAL DEFICITS AND SOMATOSENSORY EVOKED POTENTIAL (SSEP) CHANGES IN SUPRATENTORIAL BRAIN TUMOUR PATIENTS UNDERGOING NEUROSURGERY"

Background:

The patients undergoing supratentorial tumor excision usually experience unmasking of focal neurological deficits when administered sedative medications in preoperative period. Since these drugs are commonly used for procedural sedation during awake craniotomy, they can potentially confound neurological assessment conducted intraoperatively. We aimed to compare Propofol Versus Dexmedetomidine and their ability to unmask neurological deficits using clinical andelectrophysiological testing through somatosensory evoked potential (SSEP).

Materials and Methods:

In this prospective, randomized controlled double blinded study,60 patients were randomized into two groups. Group P received Propofol and Group D received Dexmedetomidine preoperatively for sedation titrated to BIS value of 60-80 and Observer's Assessment of Alertness/ Sedation score (OASS) of 4. The baseline National Institute of Stoke Scale (NIHSS) and upper limb median nerve SSEP was recorded in both the groups. Following sedation, the mean NIHSS score change along with change in amplitude and latency of SSEP were compared between groups on tumor and normal side using paired t test and repeated measures of ANOVA test, respectively. A p value <0.05 was considered significant.

Results;

Patients sedated with Propofol had a greater mean NIHSS score change of 2.63±1.16 compared to Dexmedetomidine 1.12±0.44. Also, 20 out of 21 patients in propofol groupwho had a score change of >2 also had a concomitant fall in N20 cortical amplitude on tumor side (p=0.0049) providing electrophysiological evidence that propofol unmasks focal deficits. However, only 2 patients in Dexmedetomidine showed NIHSS score change of >2 which was not associated with any change in cortical amplitude. On subgroup analysis, it was found that patients with High grade gliomas showed a change in NIHSS and fall in cortical amplitude when sedated with propofol with greater frequency compared to low grade gliomas.

Conclusion :

Propofol causes unmasking of focal deficits,especially in patients with high grade gliomas as determined by NIHSS and upper limb SSEP which can confound intraoperative clinical testing. Dexmedetomidine has emerged as a viable alternative as it does not cause unmasking of deficits and acts on subcortical level. In resource limited setting, NIHSS can be used as an alternative to SSEP as they have good correlation.

INTRODUCTION

1. INTRODUCTION

"Brain tumors" are a complex group of neoplasms arising from intracranial tissue and /or the meninges. The annual incidence of brain tumors (including primary brain tumors and lymphomas with the exclusion of spinal tumors) is around 7 per 100,000 population.(1)

Most intracranial tumors in adults arise from the supratentorial region(>80%). With the use of newer technologies such as neuro navigation and intraoperative mapping, the surgical goal aims to maximize the tumor resection while preventing any focal neurological deficits. Resection of infiltrative tumors located in eloquent areas of the brain has always been a neurosurgical challenge. Additionally, resection of infiltrative tumors without clear boundaries has resulted in a high incidence of permanent postoperative deficits (as high as 13- 17.9%).(2) Awake craniotomy has been considered beneficial in such tumors, as this enables cortical and sub cortical mapping and allows continuous neurological assessment of the patient.

Awake craniotomy presents the neuro anesthesiologist with a unique set of challenges. Choice of technique and medication varies institutionally, and the most common drugs used in the awake craniotomy are a combination of opioids like fentanyl, remifentanil, and sedation with either Propofol or Dexmedetomidine along with infiltration with local anesthetic agents.(3)

These sedative drugs ensure easy titratability, rapid onset and offset and facilitate intraoperative monitoring in awake patients. However, there have been recent reports of unmasking or exacerbation of focal neurological deficits in patients with tumors caused by sedative medication like midazolam, fentanyl , Propofol and, Dexmedetomidine as reported by Gary D et al.(4) Since these are the medications that

are commonly used during awake craniotomy, concerns regarding them producing transient focal neurological deficits intraoperatively and potentially confounding neurological assessment is of grave concern. Also, to date, these studies have reported transient focal neurological deficits subjectively through assessment of these deficits with clinical examination. There is no literature on the objective evidence that the anesthetic agents will cause focal neurological deficits. Hence, we planned the current study to use a combination of clinical neurological testing and intraoperative evoked potential using somatosensory evoked potential (SSEP) to provide objective evidence to test if the sedative agents (Propofol and Dexmedetomidine) can cause focal neurological deficits in patients with supratentorial tumors.

REVIEW OF LITERATURE

2. REVIEW OF LITERATURE

Primary brain tumors are a diverse group of neoplasm that arise from different cells in the central nervous system (CNS). Approximately, one third of the tumors are malignant, rest are benign or borderline malignant. Most of the brain tumors in adults are supratentorial in location, which arises from frontal, temporal and parietal lobes and majority(30%) are Gliomas .(1) Gliomas are primary brain tumors which arise from neuroglia stem or progenitor cells. Based on their morphological appearance histologically divided intoastrocytomas, oligodendroglioma or ependymomas.

Clinical presentation of the gliomas are usually based on their anatomical location and can present as myriad of symptoms ranging from headache, nausea vomiting to deficits in memory, speech, vision, balance etc. Gliomas are histologically divided into Grade I to Grade IV according to World Health Organization criteria (WHO) with Grade I tumor having the best prognosis,mostly occurring in children and Grade IV gliomas, also known as Glioblastoma Multiforme (GBM) having worst prognosis with median survival of only 12-18 months.(5)

Over the years there has been cumulative evidence that maximal surgical resection in all histopathological grades of gliomas is the best mode of treatment and has been associated with improved patient survival (5). Glioma resection has proven to be technically challenging because of its infiltrative nature and predominant affection of white matter tracts. Hence, the surgeon should strike a balance between maximal oncological benefit (by maximizing extent of resection) and best functional outcome which is the cornerstone in treatment of gliomas residing in eloquent areas of the brain.

Management of gliomas in eloquent areas of the brain:

With the advent of better imaging techniques and development in neuropsychological testing, there have been improvement in methods used to detect / reliably predict the functional outcome of patient undergoing resection of tumors in eloquent areas of the brain.

Methods used to minimize functional disability include:

Imaging techniques

(1) Functional MRI (fMRI)- is based on the principle that neuronal activity alters cerebral blood flow(CBF).During a particular neuronal activity, such as speech or finger tapping there is increase in ratio of oxy to deoxyhemoglobin . This event can be detected by blood oxygen level dependent (BOLD) signal. The resultant image is then superimposed on normal MRI image to locate the eloquent cortex.(6) In Gliomas , tumor induced distortion of vasculature may alter BOLD signal and functional MRI.(7) Despite its clear cut advantages it is used only as supplement to intraoperative mapping .Sensitivity and specificity of functional MRI is 81% and 53% respectively. (8)

(2) Diffuse tensor imaging (DTI)- yet another MRI based technique which helps to delineate white matter tracts and forms cornerstone in resection of gliomas. However, it is associated with its own shortcomings which include inability to provide functional information and lack of spatial resolution .(7)

(3)Magnetoencephalography (MEG)-This technology is useful in detection of cortical magnetic field produced with neuronal activation during higher cognitive processes. In addition to being non invasive, this method is also beneficial to detect synchronized neuronal currents rather than relying on surrogate such as functional

MRI which is based on neurovascular coupling. Despite its obvious advantage, it is not widely available, very expensive and requires heavily shielded room to prevent distortion of artefacts by outside sources.(7)

***(4) Transcranial magnetic stimulation*-**Navigated transcranial magnetic stimulation is newest and most promising modality available. It involves a giant electromagnetic coil which is held against the forehead and magnetic pulses are administered. These magnetic pulses induce small electric currents which stimulate the selected cortex. It has gained popularity as it is akin to direct intraoperative cortical stimulation. However, this technology is relatively novel and requires validation studies especially in aspects of language mapping.(9)

Intraoperative Brain Mapping:

***(1)Mapping of motor function by direct electric stimulation (DES)*-**In lesions located in motor cortex, motor mapping can be accomplished either using a handheld probe or a cortical grid array.

DES is performed using monopolar or bipolar electrode on cortical surface with typical current frequency of 60 Hz and current of 1 mA. Alternatively, motor strip can be identified using phase reversal of SSEP.

***(2)Mapping of functions using awake craniotomy*-** Unlike for motor function, assessment of speech can be done with awake craniotomy. Awake craniotomy takes advantage of lack of sensation of brain itself. Scalp block with local anesthetic is given and the skin incision, bone drilling and dural opening is all done when patient is under light, reversible intravenous anesthesia.

After the patient is awakened, space occupying lesions is resected with monitoring of various functions (such as motor or speech) real time. If function

changes during surgical manipulation, the resection is stopped and surgical plan revised. Cortical mapping with Direct Electric Stimulation (DES) can also be done under awake anesthesia. However, it carries high risk of intraoperative seizures.

Intraoperative brain mapping has been shown to have significant impact on surgical and oncological outcome. Comparison of two cohorts of patients undergoing low grade glioma resection with or without mapping revealed higher rate of permanent neurological deficits(17 Vs 6.5%) and lower rate of gross total resection (6 vs 24.5%)in patients without intraoperative mapping, according to a study conducted by Daffau et al .(10) A systemic review done to analyze the impact of intraoperative mapping on resection of gliomas also revealed increased rates of gross total resection (75 Vs 58%) and lowered occurrence of severe late neurological deficit (3.4 Vs 8.2%).(11)

Hence, the gold standard for resection of tumors in eloquent areas of brain is by awake craniotomy with or without direct electric stimulation.

Various techniques used during awake craniotomy are

(1) Asleep-awake-asleep.
(2) Asleep-awake.
(3) Awake throughout/conscious sedation.(12)

In a recent survey conducted in United Kingdom to determine the preferred technique of anesthesia for awake craniotomy it was found that-35% prefer ‘asleep-awake’,35% prefer ‘asleep-awake-asleep’ and 30% prefer awake throughout or sedation only approach. However,there is no consensus as to which is the best technique.(13)

The most commonly used drugs for conscious sedation during awake craniotomy are Propofol and Dexmedetomidine.

PROPOFOL:

Propofol or 2,6 di isopropyl phenol is the most commonly used intravenous induction agent. Its favorable pharmacokinetic and pharmacodynamic profile has made it the most widely used anesthetic agent. Rapid smooth induction ,short context sensitive time, rapid terminal half-life and low incidence of postoperative nausea and vomiting (PONV) is among the various benefits of Propofol.(14) Its application has extended to field of ambulatory surgery, ICU sedation and providing conscious sedation in patients undergoing diagnostic or therapeutic procedures.(15,16,17)

Drug formulation

Propofol is acidic in nature with pka=11. Due to its high lipophilicity it is formulated as 1% aqueous solution (10mg/ml) in an oil -in-water emulsion containing egg lecithin, soya bean oil and glycerol. This formulation makes it conducive to bacterial overgrowth which has been reduced by chelating agent like di sodium edetate. Propofol cause pain during injection which can be reduced by coadministration of lignocaine .(14)

It has very short distribution half-life of 2-8 minutes. It is rapidly metabolized in the liver by conjugation to glucuronide and sulphate, producing water soluble compound which is excreted mainly by the kidney. Clearance of Propofol is greater than hepatic blood flow suggestive of additional extrahepatic metabolism. The context sensitive half- life of Propofol infusion of 8 hours is less than 40 mins, hence emergence from Propofol is rapid even after long infusions.(14)

***Effect on central nervous system (CNS)*:**

Its predominant hypnotic action is mediated by binding to beta subunit of GABA-A receptorscausing opening of chloride channels causing hyperpolarization of neurons. Propofol also reduces intracranial pressure, cerebral blood flow and oxygen requirements. It has predominant anti convulsive effect at high infusion dosage and produces burst suppression on electroencephalography(EEG). It is used to terminate status epilepticus due to its anticonvulsive property.(14)

Effect on Cardiovascular system (CVS):

Propofol reduces systemic vascular resistance, cardiac contractility and preload. It also produces secondary increase in heart rate due to baroreceptor mediated compensatory mechanism in response to reduction in cardiac output and systemic vascular resistance. Usage of Propofol is poorly tolerated in patients with impaired left ventricular function due to the above properties.(14)

Effect on Respiratory system (RS):

Propofol produces profound respiratory depression and blunting of airway reflexes during intubation /laryngeal mask airway insertion without the need for muscle relaxants.(14)

Toxic effects:

Prolonged infusion of high doses of Propofol causes "Propofol infusion syndrome" characterized by metabolic acidosis, rhabdomyolysis, renal failure , lipaemia and cardiac failure .Guidelines recommend maximum Propofol infusion rates of 4.8 ml/kg/hour for long term sedation in ICU patients.(18)

Effect of Propofol on Somatosensory evoked potential

Propofol causes no effect on amplitude and <5% increase in latency. A dosage of Propofol as high as 2.5 mg/kg had no change in cortical (N19) or subcortical amplitude (N9,P13). Hence ,it has been used extensively for intraoperative neuromonitoring.(19)

DEXMEDETOMIDINE:

Dexmedetomidine is an alpha-adrenergic agonist. It has clinical applications as a sedative, anxiolytic, sympatholytic and has minimal effect on respiratory depression.(20) Dexmedetomidine has been used in intensive care units and perioperatively. It can be used as an anesthetic and opioid sparing agent,for premedication (0.33-0.67 μg/kg) 15-20 minutes before the procedure, for the purpose of sedation in ICU, post-operative analgesia and during procedures like awake fiberoptic intubation,radiological investigations and adjunct to regional anesthesia. In neuro anesthesia, it has been used in surgeries like awake craniotomy.

Drug formulation

Dexmedetomidine is the dextro-enantiomer of medetomidine which is available commercially as a water soluble HCl salt. For procedural sedation , a loading dose of 1μg/kg/hour with maintenance infusion of 0.2-0.7μg/kg/hour for ICU sedation.(20)

Dexmedetomidine is highly protein bound with more than 90% of drug binding to both albumin and alpha -1 glycoprotein. Mainly eliminated via bio-transformation in the liver. It has hepatic extraction of 0.7.(21)It undergoes direct N-glucuronidation and hydroxylation by cytochrome P450. These metabolites on conversion have weak affinity to alpa-2 receptors and hence considered inactive. It

has an elimination half-life of 2.1-3.1 hours in healthy volunteers. Clearance is marginally affected by hypoalbuminemia but impacted by change in hepatic blood flow secondary to changes in cardiac output.(21)

Effect on Cardiovascular system(CVS):

Dexmedetomidine is usually administered in a loading dose of 0.5-1 µg/kg in first ten minutes and continued as infusion of 0.2-0.7 µg/kg/hr. The initial loading dose is usually associated with hemodynamic perturbations which include bradycardia, hypo or hypertension.

The hypertensive effect is most commonly observed following loading dose is due to vasoconstrictive effect of Dexmedetomidine. Hypotension and bradycardia are associated with large loading doses.

During maintenance usually a lower mean arterial pressure and low heart rate is observed.(20)

Effect on Central nervous system(CNS):

Dexmedetomidine has analgesic, anesthetic sparing, sedative and sympatholytic effect. It has both spinal and supraspinal analgesic effect. Dexmedetomidine activates the alpha 2 adrenergic receptor which mediates activation of inwardly rectifying potassium gated channel causing hyperpolarization of the membrane and inhibits neuronal firing in spinal cord specifically in the substantia gelatinosa. It also reduces the influx of calcium ions and inhibits neurotransmitter release.(20,21)Nor adrenergic neurons in locus coeruleus have high density of alpha 2 receptors. Hyperpolarization cause by activation of these receptors thus inhibit them from firing.Inhibition of firing leads to release of GABA from preoptic and tuberomammillary nuclei which in turn releases histamine in

cortical and subcortical pathway. This inhibition is the main mechanism through which it results in drug's sedative effect. Analgesic effect is also due to modulation of neuro transmitters in locus coeruleus. Research suggests that Dexmedetomidine converges on natural sleep pathway to exert its sedative action. (22)This unique state has been utilized during awake craniotomy to balance deep level of sedation during painful and stimulative operating procedures on one hand and maximum cooperation of the patient during mapping of eloquent areas on the other. This state has been given the term "collaborative sedation".(23,24)

Effect on Respiratory system(RS):

Dexmedetomidine causes minimal respiratory depression with preservation of ventilatory response to CO_2.The frequency of respiratory rate increases with decreasing tidal volume as a compensation. Hypercapnic arousal similar to natural sleep has been observed with Dexmedetomidine sedation.(21)

Effect of Dexmedetomidine on SSEP:

Dexmedetomidine affects SSEP minimally at sedative doses.(19)

N. Goettel et al conducted a prospective randomized double blinded trial to test the efficacy and safety of using Dexmedetomidine versus Propofol - Remifentanil infusion for conscious sedation in patients coming for supratentorial surgeries during awake craniotomy .They concluded that there was no difference in quality of brain mapping and level of sedation between the two groups however, Dexmedetomidine group was associated with fewer respiratory adverse events.(25) This study also noted that Dexmedetomidine infusion is associated with common cardiovascular side effects like hypotension(45%) and bradycardia(14%) which required medical intervention in 10% and 3% of the patients , respectively.(26,27,28)

Dexmedetomidine produces sedation by its action on locus coeruleus hence it does not have any cortical action. This hinders the monitoring of depth of sedation of Dexmedetomidine using depth of anesthesia monitors which are based on processed EEG like BIS. Due to this shortcoming we used Observer assessment of alertness/sedation (OAA/S)system which is a subjective scoring system with low inter individual variability based on clinical information .(29)

Unmasking of neurological deficits by sedatives:

In 1992, Cucchira commented on a concept called "Differential awakening". He noted that patients with cerebral ischemia/mass lesion had a delay in return of motor function. It returned after 10-30 minutes unlike surgical deficits which resolved transiently. He put forward a theory that probably there are secondary pathways that compensate for and accomplish the function of destroyed neurons which are functional in awake state but are unmasked in patients with residual sedation.(30)

Thal et al, in 1996, studied the effect of fentanyl versus midazolam on motor function of the patients with supratentorial lesion /carotid disease. He noticed the patient who developed motor deficits 3 months prior to surgery were more susceptible compared to patients with chronic deficits. He also hypothesized that since the mechanism of action of these two drugs were different it was due to central, non specific effect of the drug, as opposed to drug specific effect as proposed by our study. (31)

Lazar et al in 2003,applied the same principle in patient with stroke syndrome whose symptom had subsided. His study included 8 patients (5 with left sided and 3 right sided cerebral infarct)who participated in the trial. After administration of

midazolam, the patients with left hemispheric stroke developed right sided hemiparesis but showed no neglect. The patients with right cerebral stroke showed re-emergence of left hemiparesis and left visual neglect but no aphasia. All patients returned to baseline within 2 hours. (32)

Nan Lin et al ,in 2016 did a single blind, randomized trial in 124 patients(out of which 90 patients did not have any baseline deficits). In this study they used different drugs that act on different receptor or subunits and titrated to same level of sedation in patients with supratentorial mass lesion to determine whether they have a comparableeffects on neurological signs as assessed by NIHSS. Four drugs which are used commonly in clinical practice- midazolam, fentanyl, Propofol and Dexmedetomidine. Dexmedetomidine produced least effect of the four sedatives.(33)

In an editorial review, the above phenomena was mentioned as "pharmacological stress test to the brain" which gives us insight on previous deficits, probable consequent neurological changes and clinical vulnerability of such patients suspected with neuropathology.(33)

MODIFIED OBSERVER ASSESSMENT OF ALERTNESS/SEDATION (OAA/S)

The Observer Assessment of Alertness/Sedation (OAA/S) was a scale developed to measure the level of sedation in patients. Responsiveness is graded over a 6point scale and this can be performed by clinician administering the sedation which offers ease of titration of the sedative.

6-Agitated

5-Responds when spoken to in normal tone (alert)

4-Lethargic response to name when spoken in normal tone

3-Responds only after name is called loudly or repeatedly

2-Responds only after mild prodding or shaking

1-Does not respond even to mild prodding or shaking

0-Does not respond to deep stimulus.

Chernik et al, evaluated the validity and reliability of OAA/S score in a set of 18 patients sedated with midazolam vs a placebo and the results obtained by the study showed that OAA/S has good interobserver correlation.(29).

Furthermore, a study conducted by Kasuyaet al,to study the correlation of OAA/S and BIS to monitor sedation in healthy volunteers receiving Dexmedetomidine and Propofol has shown OAA/S to be a reliable indicator of sedation .They concluded that a combination of both sedative scale and BIS can provide (34)

Both BIS and OAA/S was used in our study for assessment of depth of sedation.

NATIONAL INSTITUTE OF HEALTH STROKE SCALES (NIHSS)

National Institute of Health Stroke Scales (NIHSS) is a systematic assessment tool that provides quantitative measure of stroke related neurological deficits. It was designed originally to measure baseline data of stoke patients in acute stoke clinic. This scale has proven to be simple, reliable and valid tool that can be applied bedside. It is a quantitative measure of stroke related deficits that spans key aspects of neurological examination -Level of consciousness, language function,neglect, visual fields, eye movement,facial symmetry, motor strength, sensation and co-ordination.A detailed score sheet can be found in Appendix.

This examination can be performed by neurologists and non neurologists after appropriate training. A study done to know the intra and interobserver reliability between neurologists and non neurologists has shown to be high and correlation coefficient was found to be 0.93 and 0.95, respectively.(35)

Nan Lin et al , also used this scoring system to quantify the deficits that developed following administration of sedative medications . Similar to our study, this scoring was done before and after administration of sedative to know the unmasking of deficits .(33)

Since NIHSS scoring system has good interobserver reliability even among non neurologists it was used in our study. Furthermore we also measured NIHSS post surgicalresection .

SOMATOSENSORY EVOKED POTENTIAL (SSEP):

Evoked potential are signals produced in central nervous system in response to sensory stimuli (visual, auditory or sensory). Somatosensory system comprises of dorsal column and spinothalamic tract. The dorsal column-lemniscal pathway is involved in mechanorecepetioni.e, tactile object recognition, localization, detection of vibration and joint position. They also form the anatomic-functional substrate which can be evaluated through somatosensory evoked potential (SSEP).(36)

In 1982,Guerreiero and Ehrenberg, presented the first Brazilian paper on three cases of SSEP. They proposed that SSEP is a unique, non invasive method which can be used to detect abnormalities in somatosensory pathway and especially useful in patients with multiple sclerosis and brain death.(37)

Evoked potentials, have been developed as a complimentary to neurological examination to detect abnormal conduction through sensory pathway especially

when there is ambiguity in history and physical examination revealing subclinical involvement of somatosensory pathway. They have been used widely to detect abnormalities of both central and peripheral nervous system and unlike conventional nerve conduction studies which help to detect abnormalities in distal segment of peripheral nerve, SSEP studies help to assess the entire length of afferent pathway.

Sensory pathways:

The dorsal column deals with fine touch,2-point discrimination, conscious proprioception and vibration sense from the body. There are three order neurons that orchestrate the transmission of sensory signals from skin and joints to sensory cortex. The cell body of first order neuron is a pseudo unipolar ganglia which comprise of peripheral (distal) and central (proximal) axonal process. The distal portion of axons receive various sensory input from receptors associated with dorsal column.

Receptors are classified into two types:

1) Tactile mechanoreceptors including Meissner's corpuscles and free nerve endings which are concerned with fine touch and two-point discrimination. Pacinian corpuscles deal with position and vibration sense.
2) Conscious proprioception including muscle spindles, Golgi tendon organs (GTO) which detect muscle length and contraction change, also delivers information of axial position to central nervous system.

After receiving the sensory stimulus, the central (proximal) axons enter the dorsal root ganglion through medial dorsal root entry zone without synapsing to form the fasciculus cuneatus and fasciculus gracilis which carry sensory information form upper and lower limbs respectively. Thereafter, they synapse with nucleus cuneatus and nucleus gracilis in the caudal medulla.

Both nucleus gracilis and cuneatus form second order neurons in dorsal column-medial lemniscal pathway. The internal arcuate fibers on the contralateral side come together to form internal arcuate fibers of medial lemniscal pathway. They terminate at Ventroposterior lateral (VPL) nucleus of the thalamus. VPL are third order neurons which project laterally out of the thalamus and course through internal capsule before terminating in sensory cortex located in post central gyrus.

Technique of SSEP monitoring:

SSEP requires stimulation of peripheral nerve (i.e, median or tibial nerve) and recording the evoked potential either at level of spinal cord or sensory cortex.

Stimulation:

In order to obtain a reliable SSEP, appropriate stimulation of peripheral nerve has to occur.

Electrical stimulation of peripheral nerve can be done with:

1) Disposable conductive disc electrodes.

2) Needle electrodes.

Disc/ surface electrodes are easier to place and noninvasive but are prone to easy dislodgement and have higher impedance compared to needle electrodes. EEG disc electrodes are recommended to have impedance less than 10 k ohms to prevent stimulus artefact and reduce discomfort.Needle electrodes are easier to place and with lower impedance.(38)

Site

Upper limb SSEP:

The median nerve (C6-T1) is the nerve which is most common stimulation site. It is formed by medial and lateral cords of brachial plexus and runs downwards between tendon of palmaris longus and flexor carpi radialis longus muscles. Stimulation requires a pair of electrodes i.e, Cathode(negative) and Anode (positive) pole. The cathode used for stimulation of median nerve is at the wrist placed between the flexor carpi radialis and palmaris longus 2 cm proximal to palmar crease and the anode is placed 2-3 cm distal to anode. The median nerve when stimulated adequately should cause abduction of the thumb .(38)

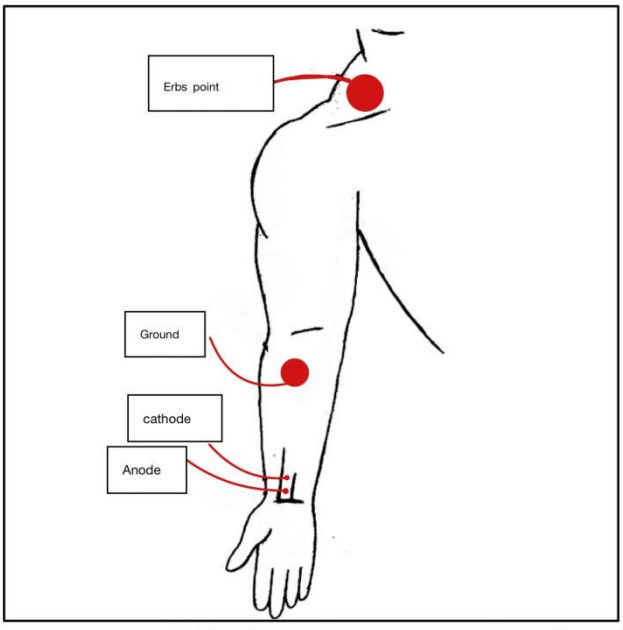


Fig 1. illustrating placement of stimulation, ground and Erb' s point electrodes.

Ulnar nerve SSEP can also be recorded intraoperatively and has greater application to look for brachial plexus injury during positioning of the patient.(39,40,41).

Lower limb SSEP:

Posterior tibial nerve(PTN) (L4-S1) is most commonly monitored to derive the lower limb SSEP. Lower limb SSEP are used to evaluate distal peripheral nerves, cauda equina, brainstem, or cerebral hemisphere. The stimulating electrode for posterior tibial nerve is placed halfway between medial border of Achilles tendon and posterior border of medial malleolus. Anode is placed 3 cm distal to the cathode. Stimulation of the PTN adequately will cause plantar flexion of the toes.(38)

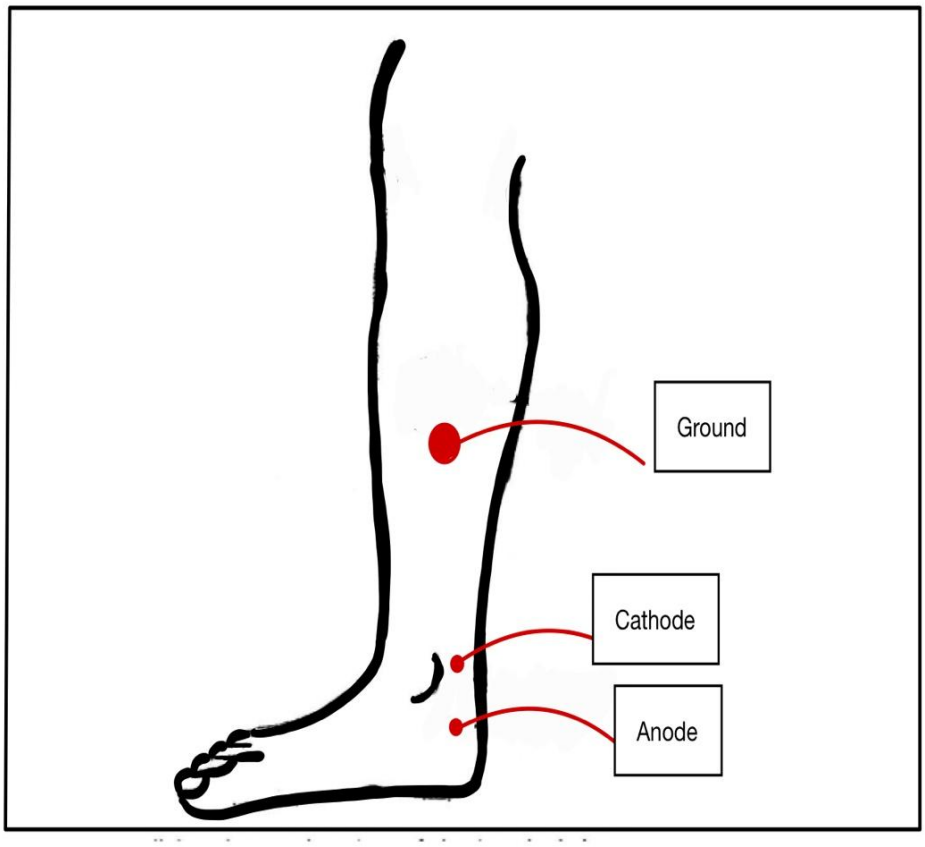


Fig.2 Illustrating placement of stimulation and ground electrodes in lower limb.

Stimulus parameters:

The guidelines according to American Clinical Neurophysiology Society (ACNS) for stimulation parameters is specific. They recommend a rectangular,

monophasic pulse delivered using constant current or constant voltage stimulator with a pulse width of 100-300µsec and stimulation rate of 3-5 Hz both in upper as well as lower limb. However, the current stimulus intensity can gradually be increased in intensity till it produces a tolerable and consistent muscle twitch.(38)

Recording of responses:

There are five obligate waveforms derived with median nerve SSEP which are designated as follows as per ACNS guidelines(42):

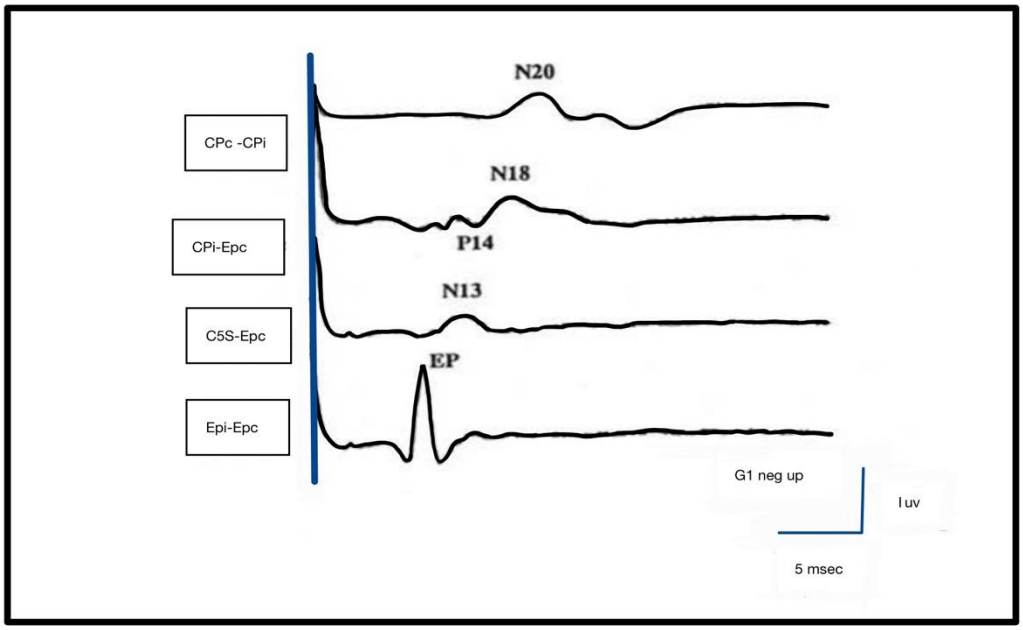


Fig 3. Illustration of recording of responses in upper limb (median nerve stimulation)

1) **EP** is propagated volley under Erb's point.
2) **N13** cervical potential recorded from dorsal neck.
3) **P14**is subcortically generated far field potential recorded from the scalp.
4) **N18**is subcortically generated far field potential preferentially recorded from scalp ipsilateral to site of stimulation.

5) **N19 reflects activation of somatosensory cortex.**

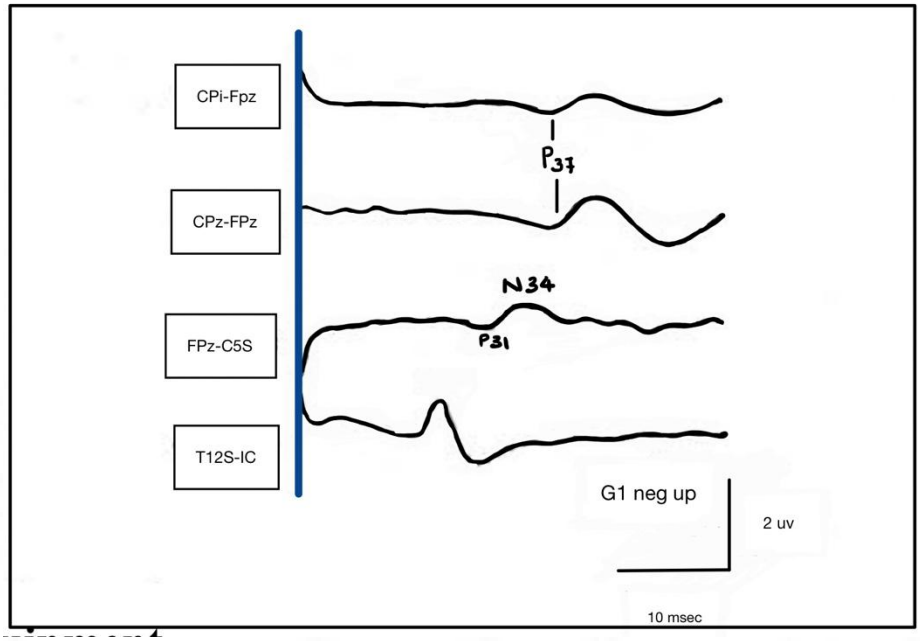


Fig.4 Illustration of recording of responses in lower limb (posterior tibial nerve stimulation)

The stimulation of posterior tibial nerve results in 3 obligate waveform designated with ACNS guidelines(42):

1) **LP**-stationary lumbar potential recorded over lower thoracic or upper lumbar spine.
2) **N34** -subcortically generated far field potential.
3) **P37**-reflects activation of somatosensory cortex.

Equipment

SSEP monitoring equipment comprises of stimulating output, recording input and an amplifier. It is mandatory for the stimulation unit to be isolated from main portion of stimulator circuitry to avoid inadvertent flow of large amounts of current in case of stimulator malfunction. An electric grounding is necessary to prevent interfering signals from power supply. The equipment also requires a band pass

width of 30-30,000Hz to record upper and lower limb SSEP. For achieving better signal to noise ratio the SSEP signals needs to be averaged over several hundred to thousand responses. The most important and frequent source of noise is usually muscle activity and patient movement .(38) The analysis time for median nerve is 50 milliseconds and tibial nerve is 100 milliseconds.(42)

Recording

Needle electrodes are generally preferred as they record larger signals than surface electrodes. The recording electrodes are placed according to 10-20 montage system (American Electroencephalographic Society 1994) is used for placement of recording electrodes. It is an international system for applying scalp electrodes to record electroencephalogram(EEG). 10-20 refers to distance between the electrodes described as 10% or 20% of distance between nasion and inion or between two auricles. Each position is denoted by a letter which indicates position of electrode and a number. Odd numbers are on the left side whereas even numbers are on the right side. The cortical responses obtained are best recorded over primary somatosensory cortex based on the nerve that is stimulated. The recording electrodes for median nerve are placed at C3´ and C4´. The recording electrodes for tibial nerve are placed at Cz´andCz´´.(42)

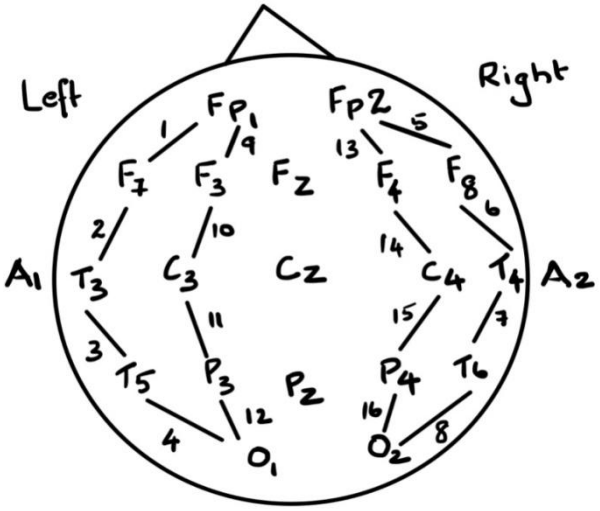


Fig 5.10-20 montage system

Alarm Criteria:

i) **Amplitude change**:A fall in amplitude of more than 50% is considered significant.(43)

ii) **Change in Latency**: Increase in latency of more than 10% is considered significant.(43)

A multi-center research done by Scoliosis Research Centre by Nuwer et al in 1995 which surveyed 51,263 patients undergoing scoliosis surgery with SSEP as the sole neuromonitoring device and found that SSEP has sensitivity of 92% and specificity of 96%.(44)

Important implications of SSEP monitoring:

Firstly, due to proximity of primary motor area to somatosensory cortex, it is assumed that any damage to motor tracts will be signaled by corresponding change in SSEP. This factor is not guaranteed.

Secondly, the blood supply of corticospinal tract differs from that of dorsal column. Hypoperfusion in the area of anterior spinal artery which affects corticospinal tract may not affect SSEP monitoring.(45)

In patients with preoperative neurological deficits, a reliable data can be obtained in 75-85% of patients.(46)

Depth of anesthesia monitors

Depth of anesthesia monitors have gained popularity due to extensive use of total intravenous anesthesia (TIVA) to facilitate intraoperative neuromonitoring. It is also used in awake craniotomy to titrate depth of sedation. Processed EEG is extensively used for the same.All depth of anesthesia monitors use processed EEG to produce a dimensionless digital number which is easier to interpret.

Raw EEG is predominantly derived from the frontal region.The EEG signal then undergoes the complex process of filtration, amplification and digitalization. This is processed by the device mathematically. Raw EEG is usually divided into segments also known as epochs. Of the different depth of anesthesia ,Bispectral index (BIS) is the most common modality.

BIS

It has a montage which picks up raw EEG signals from the frontal region and converts it into a number between isoelectric EEG (0) and fully awake (100). Its calculation algorithm includes power spectrum, bispectrum, relative activity in the beta frequency range, burst suppression activity and synchronized fast slow activity. Apart from BIS value it also displays signal quality index, burst suppression ratio, electroencephalography(EEG) and electromyography(EMG). A value between 40 and 60 indicates adequate depth of anesthesia.(47)

Rationale of the study:

Various studies done in this field have already outlined the transient worsening or unmasking on focal neurological deficits in patients with limited cerebral reserve on administration of sedation. The two current drugs most frequently used in anesthesia for conscious sedation are Propofol and Dexmedetomidine. For example, in a patient undergoing awake craniotomy which is done in patients with tumors close to eloquent areas of the brain,if patient is provided with conscious sedation, the residual sedative effects of the drugs might interfere with intraoperative evaluation of language, sensory, motor functions and destroy the purpose of keeping the patient awake.

It might also interfere in the assessment of focal neurological deficits following successful mechanical thrombectomy for stroke under sedation. Until now only one study has elucidated and proven that appearance/unmasking of focal deficits is a drug specific phenomena. Also, whether the exacerbation of deficits occur more frequently in locally aggressive like high grade gliomas in comparison to low grade glioma and correlation of the same with MRI and post operative deficits is not known. Previous studies have subjectively evaluated the deficits using NIHSS only. So, we designed this study to provide electrophysiological proof with SSEP along with correlation of the same post operatively.

RESEARCH HYPOTHESIS

Research Hypothesis-

Propofol sedation will unmask focal neurological deficits by causing a change in NIHSS score and / change in amplitude and or / latency in SSEP compared to Dexmedetomidine when given in patients with supratentorial tumors(gliomas).

Null Hypothesis-

There is no difference between Propofol and Dexmedetomidine sedation in terms of change in NIHSS score /change in amplitude and or/ latency of SSEP when given in patients with supratentorial tumors (gliomas).

AIMS AND OBJECTIVES

Objective:

The aim of this study is to assess the mild sedation effects of Propofol and Dexmedetomidine on focal neurological deficits and SSEP monitoring in patients undergoing supratentorial glioma resection surgeries.

Primary aim-

To monitor for focal neurological deficits and somatosensory evoked potential changes caused by sedation with Propofol Vs Dexmedetomidine in patients undergoing glioma resection.

Secondary aim-

To correlate the same with focal neurological deficits that occurs post operatively.

MATERIALS AND METHODS

3. MATERIALS AND METHODS

This is a prospective observational study designed to test the hypothesis that either the use of Propofol or Dexmedetomidine will cause unmasking of focal neurological deficits when administered in sedative doses to patients undergoing resection of supratentorial intra axial tumor surgeries.

Setting: Neurosurgical operation theatre (NSOT) at Sree Chitra Tirunal Institute of Medical Sciences and Technology (SCTIMST), Trivandrum, which is a specialized tertiary referral center.

Institutional Ethics Committee Approval:This study was approved by our Technical Advisory Committee and Institutional Ethics Committee registration no - SCT/IEC/1566/OCTOBER-2020.

The study was registered in the clinical trials registry of India(CTRI) with reference number CTRI/2022/02/040164.

Study period: Patients were enrolled from August 12, 2020 to February 28, 2022 for the study.

Study Design: Prospective observational case study. The total number of participants were sixty.

Patient enrolment: The patients were recruited by the investigators from the elective neurosurgical operation theater list with a primary diagnosis of supratentorial located intraaxial brain tumor namely glioma. The patients were screened for eligibility using the following inclusion and exclusion criteria. Once they were eligible written informed consent was obtained for inclusion in the study.

Inclusion criteria:

- Patients posted for elective supratentorial fronto-temporo-parietal gliomas resection surgeries.
- Age 18-65years.
- ASA grade I and II.
- No pre-operative sensory or motor neurological deficits(NIHSS-0).

  Glasgow coma scale (GCS)-14-15.

Exclusion criteria:

- Patient refusal for study.
- Patients with focal neurological deficits.
- GCS score less than 14.
- Age less than 18 years and more than 60 years.
- ASA grade III and IV.
- Pregnant or lactating women.
- Recurrent brain tumor.
- Unable to communicate, comprehend or co-operate during a neurological examination. Impaired mental status
- Presence of significant comorbidities like coronary artery disease, cardiac conduction abnormalities, COPD, systemic hypertension, diabetes mellitus, chronic renal disease.
- Drug intake like sedatives/drugs/alcohol use.

  Allergy to the study drugs.

Study Protocol:

Informed consent was taken from the patients satisfying the inclusion criteria and consenting patients were included in the study. All the patients were explained about the study protocol. Patient who met the recruitment criteria were randomly assigned into two groups of 30 each labelled as Propofol (Group P) and Dexmedetomidine (Group D). Randomization was based on computer generated random digits tableas shown in table 1 below.

Table1. Allotment of study subjects based on computer generated random digits table.

1	**P**	**11**	**P**	**21**	**P**	**31**	**D**	**41**	**P**	**51**	**P**
2	**D**	**12**	**D**	**22**	**P**	**32**	**D**	**42**	**P**	**52**	**P**
3	**P**	**13**	**P**	**23**	**D**	**33**	**P**	**43**	**D**	**53**	**D**
4	**D**	**14**	**D**	**24**	**D**	**34**	**D**	**44**	**D**	**54**	**P**
5	**P**	**15**	**D**	**25**	**P**	**35**	**D**	**45**	**P**	**55**	**D**
6	**D**	**16**	**P**	**26**	**P**	**36**	**P**	**46**	**D**	**56**	**P**
7	**D**	**17**	**D**	**27**	**P**	**37**	**P**	**47**	**P**	**57**	**D**
8	**P**	**18**	**P**	**28**	**D**	**38**	**D**	**48**	**P**	**58**	**D**
9	**D**	**19**	**P**	**29**	**D**	**39**	**D**	**49**	**D**	**59**	**P**
10	**P**	**20**	**D**	**30**	**D**	**40**	**P**	**50**	**D**	**60**	**P**

Neurophysiologists who were doing neuro monitoring, neurologists who were assessing the NIHSS of the patient and patient recruited for the study were blinded regarding the group allocation.

The day before the scheduled surgery, patient underwent a thorough pre-anesthetic evaluation, neurological examination and a baseline National Institute of Health Stroke Scale (NIHSS) score to evaluate the neurological status in terms of visual, sensory, motor function ,ataxia ,attention and language was recorded.

On the day of surgery all the patients were kept nil per oral (NPO) consisting of 8 hours for solids and 2 hours for clear liquids. No pre-operative

sedation was administered and patients were allowed to continue their routine anti epileptics drugs with sips of water. Each patient was shifted to the operation theatre after filling the WHO safety checklist. Pre induction monitors were attached which included five lead electrocardiogram, pulse oximeter ,non-invasive blood pressure(NIBP), end tidal carbon dioxide (ETCO2) and depth of anesthesia monitor i.e, Bi Spectral index (BIS) as shown in Fig. 9 and baseline values were recorded. An 18 G intravenous access was established in a peripheral vein and intravenous fluid of 2ml/Kg of Ringer's solution was started. Electrodes for somatosensory evoked potential monitoring was placed as follows:

Stimulating electrode placement consists of pair of subdermal electrodes of which the cathode is placed between the tendons of palmaris longus and flexor carpi radialis muscle,2-3 cm proximal to the wrist creaseand the anode is placed 2cm distal to the cathode or on the dorsal surface of the wrist as shown in figure below.

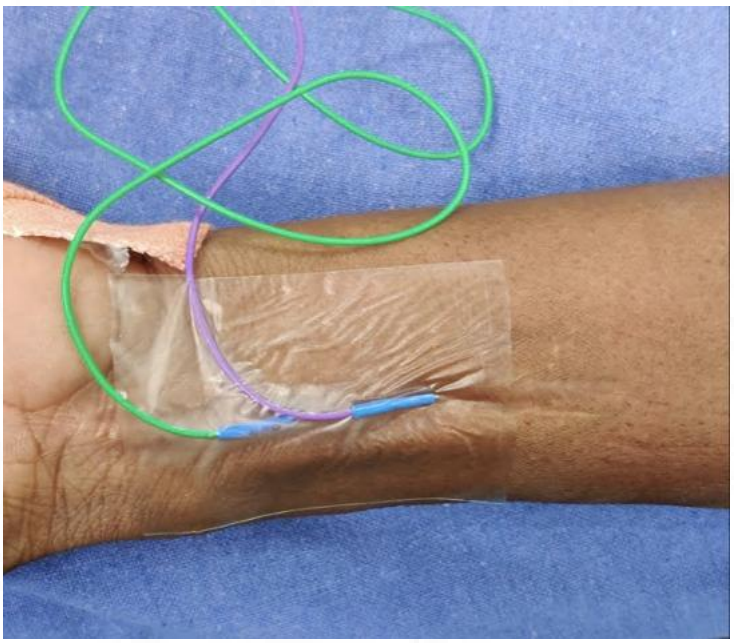


Fig 6. Placement of needle electrodes for median nerve stimulation

Subdermal needle electrodes were placed on scalp over somatosensory cortexfor recording of cortical potentials. The intradermal needle electrodes used for this study purpose was 1.5 mm in length and were 27 G (Medtronic, Xomed).The equipment used to stimulate and record SSEP was Natus Neurology XL TEK Protector 32 (Natus Medical Incorporated, Canada) monitor.

Fig 7. XL TEK Protector IONM

The needle electrodes were placed after cleaning the area with chlorhexidine and 70% alcohol solution and were secured in place using waterproof adhesive plasters.

For placement of recording electrodes 10-20 montage system was used. For recording SSEP of the upper limb; recording electrodes were placed over somatosensory cortex at the position of CP3 and CP4 along with reference (neutral) electrode at Fz. Baseline parameters were recorded.

For identifying the somatosensory cortex, the midline was marked and the coronal sutures were palpated bilaterally. Points were marked 5-7 cm behind the coronal suture and 5 cm lateral to the midline. The subdermal electrodes were placed on the marked points for C3' and C4' for left and right sides respectively and secured with plaster as shown in Fig. 6. Baseline SSEP's were recorded by stimulating bilateral upper extremities(median nerve) using needle electrode..

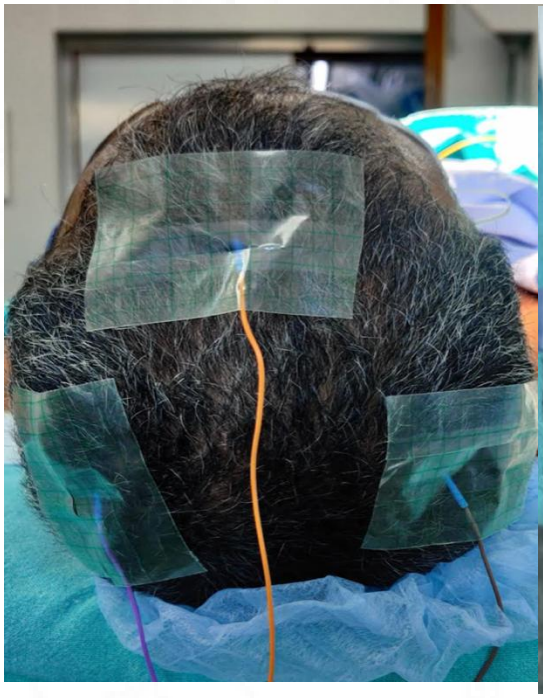


Fig.8 Placement of Scalp electrodes

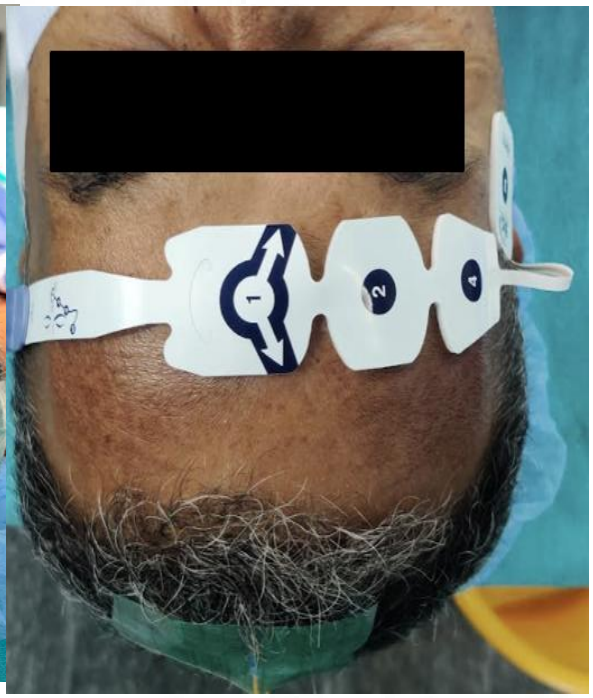


Fig.9 BIS monitor placement

A brief rectangular constant current stimuli of 0.3 microseconds duration with current intensities up to 15-25 mA applied to median nerve at the wrist at stimulation frequency of 3.17Hz.The stimulus parameters were kept constant as that used for obtaining baseline for all subsequent stimulations.

Baseline SSEP was recorded averaging 500 responses to obtain one waveform(better signal: noise ratio). The cortical and subcortical potentials (N9, P13 and N19 were recorded and the latencies and amplitudes were noted (T0).

After recording the baseline data, the sedation was initiated as per randomization which is as follows;

GROUP P-received Propofol via Target controlled infusion (TCI pump) using with effect site concentration 1.5 mcg/ml (Schnider model) over 10 minutes.

GROUP D- received Dexmedetomidine at 0.5 mcg/kg/min infusion over 10 minutes.

The end point was achieving a stable BIS valueof 60 - 80. In addition to BIS, Observer Assessment of Alertness/Sedation (OAA/S) was used in both groups to assess the desired level of sedation i.e, the patient's minimum score should be 4. Patient with the score of 4 was lethargic but obeying commands allowing NIHSS to be evaluated. If the BIS values were <60 , the drugs were temporarily stopped to allow BIS to reach 60-80 and OASS 4

At timepoint **T1** (post sedation 10 minutes) and **T2**(post sedation 15 minutes)when both BIS score was between 75-80 and OAA/S was minimum of 4,all the patients were assessed for NIHSS evaluation to determine presence of any new deficit unmasked during sedation and repeat SSEP values was recorded similar to baseline. Any patient who became over sedated (<60) or under sedated (failed to reach BIS 75-80) following 10 minutes of infusion were excluded from the study.

Based on the observations, patients were categorized into NIHSS positive and NIHSS negative -

NIHSS POSITIVE- Any change of NIHSS score> or equal to 2 after sedative administration.

NIHSS NEGATIVE-Any change of NIHSS score <2 after sedative administration.

Corresponding to NIHSS scoring, SSEP waveforms were recorded at time interval T1 and T2.

ALARM CRITERIA: Fall in amplitude of 50% or increase in latency of more than 10% was considered significant.

Following recording, general anesthesia was induced withInj Propofol 2mg/kg, Inj vecuronium 0.1 mg/kg and fentanyl 2 mcg/kg. Group P received Propofol and fentanyl as infusion for maintenance. Patient in Group D received Dexmedetomidine and fentanyl as maintenance.At the end of surgery, all the patients were reversed and extubated. Neurological assessment was done in the post operative period. NIHSS score was re-evaluated after 3 hours of shifting to ICU to assess neurological deficits in the postoperative period.

During the initial study period, vitals parameters of the patients(heart rate, systolic, diastolic and mean blood pressure, oxygen saturation by pulse oximetry) were documented and sedation was stopped if any of the following adverse events occurred during the initial period of administration of the study drugs:

1) Change in systolic blood pressure± 20% form baseline.

2) Bradycardia with heart rate<40beats/mintreated with. Inj atropine 0.6 mg i.v.

3) Tachycardia with heart rate > 120beats/min treated with fluids.

4) Fall in SPO2 <92%.

STATISTICS

A) Sample Size Calculation:

Previous studies evaluating the neurological function had shown that 30% of patients hadexacerbation /unmasking of focal neurological deficits after sedation. Hence the proportion of NIHSS change following sedation was assumed to be 30% under null hypothesis and 75% under alternate hypothesis. The significance level of test will be target at 0.05 and statistical power of 90%. Sample size in our study was calculated using universal sampling technique and was found to be thirty in each group. We recruited all consenting patients presenting for frontotemporoparietal glioma resection surgery during our study period from August 2020 to February 22 at our institute and aimed to recruit 30 patientsin each group based on our inclusion and exclusion criteria.

B) Statistical Analysis

The normally distributed data was described as mean and standard deviation with paired student t test before and after medication.

For categorical variables number and percentage was described by Fischer's exact test was used to analyze the difference between the groups.

- The baseline parameters and perioperative characteristics were using Student T test (continuous variables) or the chi square test (qualitative variables).Kolmogorov Smirnoff was done to check whether the distribution of data was normal.
- For comparing the amplitude and latency of three waveforms N9, P13 and N19 waveforms for a given group at T0,T1and T2, repeated measures of ANOVA with post hoc analysis and Bonferroni correction was used.
- To compare the values of amplitude and latency between groups at different time points T test was used.
- For comparing hemodynamic parameters heart rate and mean arterial pressure within a group at T0,T1 and T2 repeated measures of ANOVA with post hoc analysis and Bonferroni correction was used.

- To compare the values of heart rate and mean blood pressure between groups at different time points T test was used.
- For comparing BIS values between the groups t test was used.

The software used for statistical analysis was SPSS software.(Version 23, IBM, USA)

RESULTS

4. RESULTS

We screened a total on 75 patients with the diagnosis of temporoparietal gliomas over two year study period. After applying the inclusion and exclusion criteria,60 patients were found eligible and were recruited for the study. The selected patients were randomized into two groups

Group P and Group D by a computer generated random number. The following Consort Flow diagram(Fig 10) illustrates the patient recruitment and follow up details.

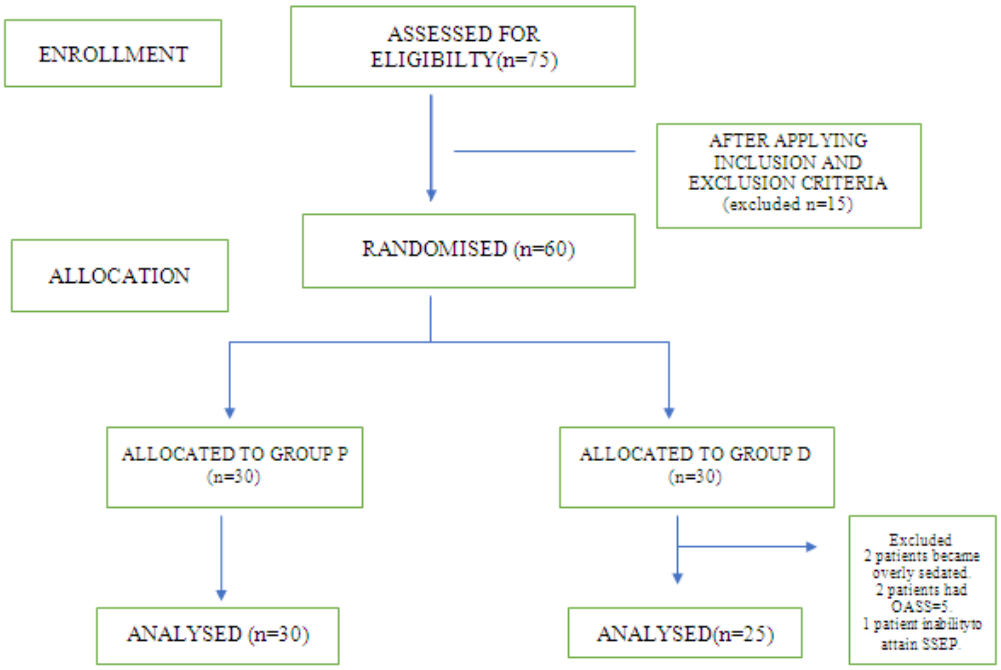


Fig-10. Consort Flow Diagram of Patient recruitment and study details

Table 2. Shows the comparison of the demographic data between the groups. (Group P=Propofol, Group D=Dexmedetomidine, p value < 0.05 significant using Student 't' test)

Variables	Group P(n=30)	Group D(n=25)	p-value
Age in years (Mean ±SD)	34.8±7.8	38.1±9.3	0.1666
Weight in kgs (Mean ±SD)	63.3±10.5	64±9.7	0.8142
Height in centimeters (Mean ±SD)	162.7±7.1	160.1±5.2	0.1247
Gender (male: female)	11:19	14:11	0.580 (Chi Square Test)
ASA Grade I n(%)	20 (66.7%)	12 (48%)	0.162 (ANOVA)
ASA Grade II n (%)	10 (33.3%)	13 (52%)	
ASA Grade III/IV n(%)	0(0%)	0 (0%)	
Diagnosis: (L) temporoparietal glioma n (%) (R) temporoparietal glioma n (%)	 18 (60.0%) 12 (40.0%)	 10 (40%) 15 (60%)	0.140
Type of tumor: HIGH GRADE GLIOMA LOW GRADE GLIOMA	 20 10	 17 8	0.91647 (Chi square test)
Duration of surgery (Mean ±SD)	207.5 ±39.4	178.9 ±64.9	0.06
Duration of anesthesia (Mean ±SD)	266.9 ±38.0	236.4 ±34	0.06
Saturation (SpO_2) % (Mean ±SD)	98.9±0.6	98.64±0.86	0.2994
Respiratory rate (breaths/minute) (Mean ±SD)	12.33±1.32	12.36±0.95	0.9247

The demographic details of the recruited patients are shown in the table 2. The mean age of patients were 34.8±7.8 and 38.1±9.3 years in Group P and Group D respectively. (p=0.16). There were more females in the Group P compared to Group D, but was not found to be significant. Moreover, there were differences in the tumor side between the groups, with more patients in Group P had tumor on left side (60%) compared to Group D (40%). However, this was not statistically significant. Other variables like weight, ASA grade, duration of surgery and anesthesia were comparable in both groups.

Table 3.Showing the comparison of the Preoperative symptoms at presentation between groups:

Pre-operative complaints	Group P (n=30)		Group D (n=25)	
	Number	Percentage	Number	Percentage
Acalculia/alexia/anomia	01	33.3%	00	0%
Focal seizures	06	20%	03	12%
Generalized seizure	07	23.3%	07	28%
Headache	23	76.67%	15	60%
Nausea	01	3.33%	0	0%
Giddiness	00	0%	01	4%
Memory loss	0	0	0	0

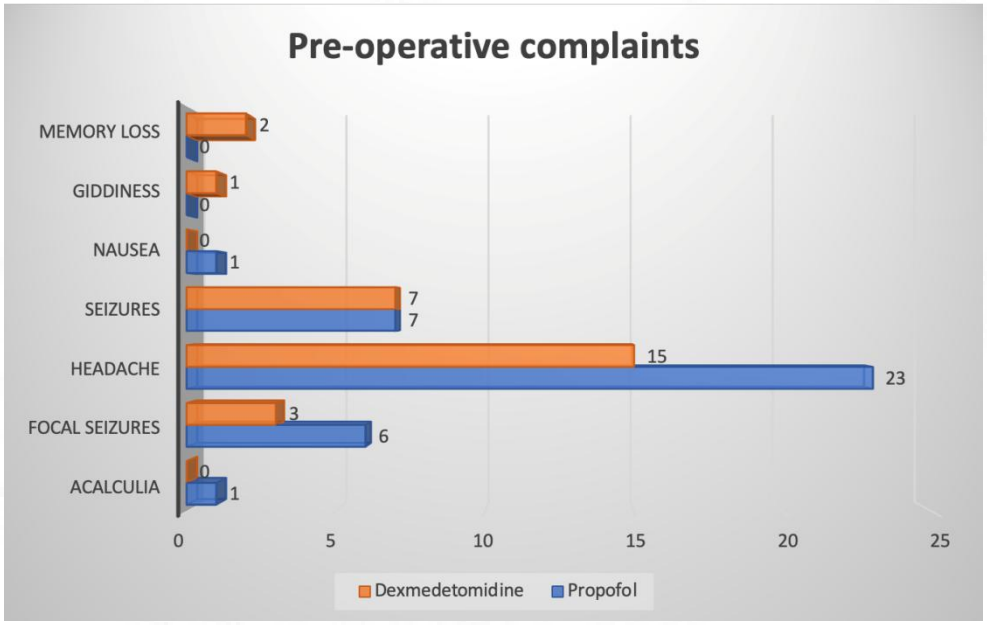


Fig 11 shows the bar diagram on the frequency of the symptoms in the study groups.

Table 3 shows the comparison of the symptoms at presentation. Headache was the most common presentation followed by seizure (focal or generalized) in both the groups. Few patients had more than one preoperative complains. None of the patients had focal motor or sensory deficits on preoperative evaluation.(table 3, Fig. 11)

Hemodynamic effects:

Table 4.1 Comparing the mean heart rate (HR) between the two groups at different time intervals. ((Group P=Propofol, Group D=Dexmedetomidine, p value < 0.05 significant using repeated measures of ANOVA)

Heart rate (beats/min)	Group P Mean± SD	Group D Mean± SD	P value
T0 (baseline)	77.8±8.1	83.7±8.1	0.0101*
T1	69.9±6.9	64.3±6.8	0.0046*
T2	68.2±6.9	58.8±6.7	<0.0001
P<0.05 (ANOVA)	0.0001*	0.0001*	

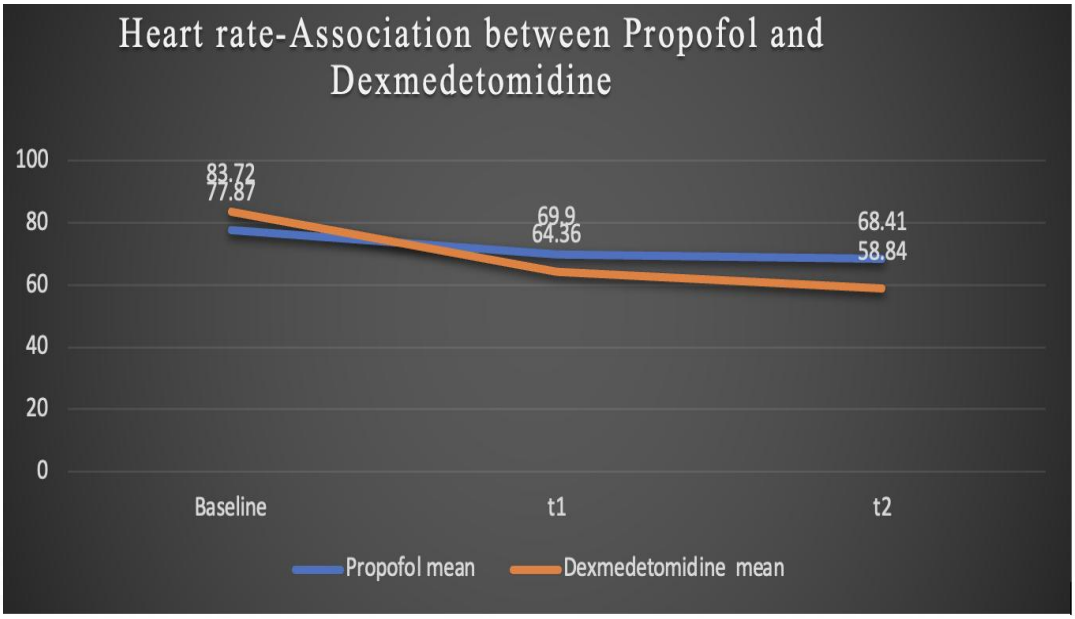


Fig 12 Comparing the mean heart rate (HR) between the two groups at different time intervals

Table 4.1shows the comparison of the mean heart rate between the groups. The HR was higher in group D at baseline (T0); however, there was a significant fall in the HR in both groups from baseline till T2. We also noted that the fall in HR in Group D was higher than Group P and was significant(Table 4.1,Fig 12)

Table 4.2 Comparing mean blood pressure between two groups at different time intervals (Group P=Propofol, Group D=Dexmedetomidine, p value < 0.05 significant using repeated measures of ANOVA)

Mean blood pressure (mm Hg)	Group P Mean +SD	Group D Mean +SD	P value
T0 (baseline)	91.3±6.9	87.8±5.2	0.0532
T1	84.9±5.6	77.6±6.9	0.0001*
T2	86.5±6.5	77.4±9.9	0.0001*
P<0.05 (ANOVA)	0.0001*	0.0001*	

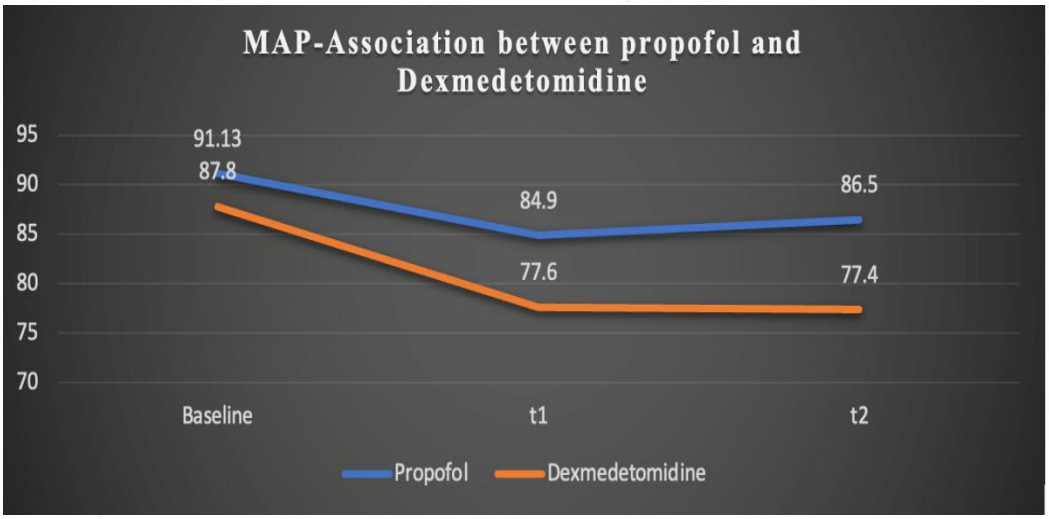


Fig.13 Comparing mean arterial blood pressure at different time intervals .

As shown in table 4.2 There was no significant difference in the mean blood pressure in both the groups. However, there was a statistically significant fall in MAP in both groups at T1 and T2 time periods, but the mean fall was approximately 5 mm in Group P compared to 10 mm Hg fall in Group D.(Table 4.2,Fig.13)

Table 5: Shows the comparison of the Bispectral index (BIS) and Observer's Assessment of Alertness /Sedation scale (OASS) between the groups. (Group P=Propofol, Group D=Dexmedetomidine, p value < 0.05 significant using repeated measures of ANOVA)

	BIS			OASS		P value
	Group P (n=30)	Group D (n=25)	P value	Group P (n=30)	Group D (n=25)	
T 0 (baseline)	96.67±3.25	98.2±2.25	0.0519	5	5	NS
T 1	73.47±4.85	77.96±4.89	0.0013*	4	4	NS
T2	73.2±5.12	78.32±4.57	0.0003*	4	4	NS
(p value)	<0.00001*	<0.00001*				

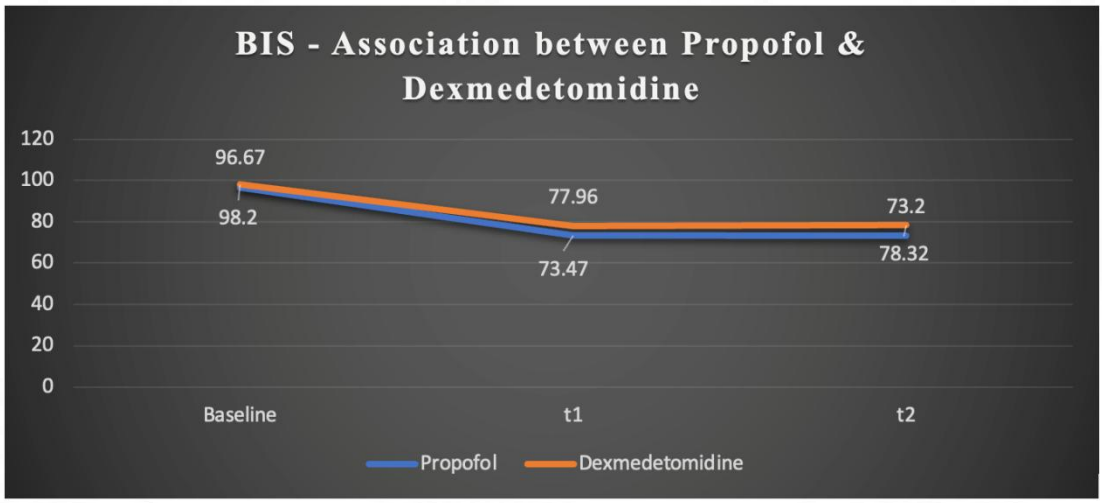


Fig 14 .BIS values at different time intervals .

Baseline BIS was comparable between Group P and Group D at the beginning of sedation at time interval T0. Both groups consistently showed a fall in BIS value from above 90 to values between 60-80. However, BIS values recorded at time interval T1 and T2 in Dexmedetomidine group was slightly higher compared to

Propofol. Since BIS is not a reliable indicator during Dexmedetomidine sedation, it was supplemented with clinical scale to assess Depth of sedation -Observer's Assessment of Alertness /sedation scale (OAA/S). All patients were sedated to achieve an OAA/S score of 4 at T1 and T2 interval**.** Patients who did not attain a score of 4 or those who became overly sedated were excluded to make both the groups comparable.(table 5, Fig 14)

Table 6: Shows the comparison of the National institute of Health Stroke scale (NIHSS) score between the groups.

Mean and standard deviation of NIHSS score change in relation to the two study groups from baseline :(Group P=Propofol, Group D=Dexmedetomidine, p value < 0.05 significant using repeated measures of ANOVA)

	Group P(n=30) (Mean ±SD)	**Group D (n=25) (Mean ±SD)**	**P value**
Baseline (T0)	0	0	**NS**
Post sedation (T1)	2.6±0.2	1±0.1	<0.0001*
Post sedation (T2)	2.6±0.1	1±0.2	<0.0001*
NIHSS score change (Mean ±SD)	2.63±1.16	1.12±0.44	

The NIHSS was similar at baseline. The score changed significantly in Group P patients with Propofol sedation compared to Group D.($p<0.0001$). Moreover, we also noted that the number of patients having NIHSS score change >2 was higher in Group P (70%) compared to Group D(8%). As demonstrated in table 7 , 21 out of 30 patients sedated with Propofol showed NIHSS score change of >2 as compared to Dexmedetomidine group which showed a score change of >2 in only 2 patients out of 25. All the patients showed a score change of 1 from the baseline due to sedation.(table 6).

Table 7: Shows the Percentage distribution of sample according to NIHSS score change that occurred in Propofol group and Dexmedetomidine group.

NIHSS score change	Group P (n)	Percentage	Group D (n)	Percentage
1	9	30%	23	92%
2	0	0%	1	4%
3	14	46.6%	1	4%
4	7	23%	0	0%

Table 8:Intraoperative change in NIHSS(specifications): (Group P=Propofol, Group D=Dexmedetomidine)

Intraoperative change (specifications)	Group P COUNT (n)	Percentage (%)	Group D COUNT (n)	Percentage (%)
Aphasia	3	10%	0	0%
Articulation	3	10%	0	0%
Motor	12	40%	1	4%
Ataxia	15	50%	1	4%
Sensory	3	10%	0	0%
Orientation	6	20%	0	0%

Table 8. shows the details of change in NIHSS score in both Propofol and Dexmedetomidine group. Group P (patients sedated with Propofol) had maximum score change in form of development of motor deficits (40%) and ataxia (50%) of the patients. 10% of patients also showed difficulty in articulation and 10% became Aphasic. 20% of patients had loss of orientation. In contrast, patients sedated with

Dexmedetomidine Group D did not show much change in NIHSS score. Only one patient (4%)developed a drift in upper limbs during examination and one patient (4%)demonstrated inability to perform finger –nose test.

Changes in Upper Limb Somatosensory Evoked Potentials (SSEP):

The changes in the latency and amplitude of the SSEP waveform in between the groups were analyzed. Also, the changes in SSEP were compared between the tumor and non tumor hemisphere.

Table 9.1 Table comparing mean amplitude and latency of N9 waveform at T0,T1 and T2 on tumor side and non-tumor side inter and intragroup in upper limbs: (Group P=Propofol, Group D=Dexmedetomidine, p value < 0.05 significant using repeated measures of ANOVA)

N9 Amplitude (microvolts)	N9 tumor side			p value	N9 non tumor side			p value
	t 0	t 1	t 2		t 0	t 1	t 2	
Group P	0.30 ±0.12	0.37± 0.51	0.37± 0.46	0.73	0.26±0.14	0.26± 0.12	0.27± 0.14	0.97
Group D	0.34±0.14	0.29± 0.12	0.29±0.13	0.26	0.45±0.50	0.38± 0.45	0.39± 0.48	0.85
p value	0.2589	0.4472	0.4042		0.0514	0.1661	0.1971	
N9 Latency (in milliseconds)								
Group P	9.16± 0.39	9.11± 1.22	9.17± 1.29	0.97	9.18±0.29	9.38± 0.29	9.5± 0.34	0.75
Group D	9.30± 0.39	9.54 ±0.44	9.74 ±0.44	0.002*	9.27±0.27	9.53± 0.37	9.74 ±0.38	0.002*
p value	0.1907	0.1004	0.0399		0.2424	0.0978	0.2238	

There was no significant change in mean amplitude of N9 waveform at T0(baseline) ,T1 and T2 in both Group P and Group D on the tumor as well as non-tumor side. There was no difference in N9 mean amplitude as well as mean latency between the two groups (Group P and Group D) both on tumor and non-tumor side.

There was a statistically significant increase in N9 latency at time intervals T1 and T2 compared to baseline on both the tumor as well as non-tumor side in Group D. However, it was observed that this increase in subcortical latency was small (0.2 ms), even though statistically significant did not satisfy clinical criteria for prolonged latency (i.e, increase > 10% from the baseline).

Table 9.2Table comparing mean amplitude and latency of P13 waveform at T 0, T1 and T2 on tumor side and non-tumor side inter and intragroup. (Group P=Propofol, Group D=Dexmedetomidine, p value < 0.05 significant using repeated measures of ANOVA)

P13 Amplitude (microvolts)	P13 tumor side			p value	P13 non tumor side			p value
	t 0	t 1	t 2		t 0	t 1	t 2	
Group P	0.30 ±0.21	0.40± 0.53	0.39± 0.48	0.61	0.26± 0.11	0.25± 0.11	0.27± 0.10	0.85
Group D	0.29± 0.21	0.25 ±0.20	0.24 ±0.19	0.69	0.32± 0.24	0.33± 0.23	0.32± 0.23	0.66
p value	0.7208	0.1872	0.1481		0.2766	0.0970	0.2866	
P13 Latency (in milliseconds)								
Group P	13.07±1.89	13.21±1.97	13.35±2.06	0.86	12.68±0.87	13.00±0.88	13.19±1.01	0.148
Group D	12.74±0.83	13.15±0.73	13.32±0.87	0.042*	13.26±0.40	13.45±0.39	13.58±0.37	0.008*
p value	0.4219	0.8860	0.9461		0.1900	0.147	0.0546	

There was no significant change in mean amplitude of P13 waveform at time intervals T0,T1 and T2 in both Group P and Group D on tumor as well as non-tumor side. There was no significant difference in mean amplitude and mean latency of P13 waveform between two groups both on tumor and non-tumor side. There was a statistically significant increase in P13 latency at time interval T1 and T2 compared to baseline on both tumor as well as non-tumor side in Group D. However, it has been observed that this increase in latency (0.2 ms) even though statistically significant did not satisfy the clinical criteria for prolonged latency (i.e, increase >10% from the baseline). Moreover , the change seen in latency could be due to prolonged latency of N9 by 0.2 ms seen in Group D.

Table 9. 3 Table comparing mean amplitude and latency of N19 waveform at T0,T1 and T2 on tumor side and non-tumor side inter and intragroup (Group P=Propofol, Group D=Dexmedetomidine, p value < 0.05 significant using repeated measures of ANOVA)

N19 Amplitude (microvolts)	N19 tumor side			p value	N19 non tumor side			p value
	t 0	t 1	t 2		t 0	t 1	t 2	
Group P	1.75±0.71	1.02±0.71	0.96±0.70	0.000039*	1.70±0.63	1.58±0.55	1.52±0.59	0.47
Group D	2.06±0.89	1.74±0.80	2.45±4.05	0.58	1.90±0.84	1.63±0.77	1.52±0.80	0.230
p value	0.1566	0.0009*	0.0039*		0.3180	0.7804	1.000	
N19 Latency (in milliseconds)								
Group P	22.2±3.64	22.38±3.73	22.58±3.84	0.92	22.77±0.58	22.96±0.49	23.05±0.55	0.0940
Group D	21.01±0.72	21.62±0.79	21.55±1.88	0.173	22.59±0.62	22.59±0.60	22.55±1.56	0.37
p value	0.1142	0.3224	0.2267		0.0167	0.6809	0.8900	

At baseline the amplitude and latency of N19 was similar in both the groups. However, there was a significant fall in N19 cortical amplitude on tumor side at T1 and T2 interval from baseline in Group P (intragroup) . This fall in amplitude was statistically(p=0.000039) and clinically significant (i.e, >50% from the baseline) on the tumor side in Group P. There was a statistically significant difference in N19 cortical amplitude on the tumor side in Group P as compared to Group D at T1 and T2. There was no significant difference in mean amplitude on non-tumor side between two groups .There was also no difference in mean latency of N19 waveform between two groups both on tumor and non-tumor Side.

Table 10.1 Association between NIHSS score change and change in amplitude on tumor side at time interval T1:

Side involved	SSEP Parameter	Group P NIHSS > 2	Group D NIHSS > 2	Chi square value	p value
N9 tumor side	Fall in amplitude <50% from baseline	21	2	---------	--------
	Fall in amplitude > 50% from baseline	0	0		
P13 tumor side	Fall in amplitude <50% from baseline	20	2	0.1	0.751 NS
	Fall in amplitude > 50% from baseline	1	0		
N19 tumor side	Fall in amplitude <50% from baseline	3	2	7.886	0.0049 *
	Fall in amplitude > 50% from baseline	18	0		

(Chi square test - * significant, NS – not significant at p value < 0.05)

Table 10.2 Association between NIHSS score change and change in amplitude on tumor side at time interval T2:

Side involved	SSEP Parameter	Group P NIHSS > 2	Group D NIHSS > 2	Chi square value	p value
N9 tumor side	Fall in amplitude <50% from baseline	21	2	---------	--------
	Fall in amplitude > 50% from baseline	0	0		
P13 tumor side	Fall in amplitude <50% from baseline	21	2	---------	--------
	Fall in amplitude > 50% from baseline	0	0		
N19tumor side	Fall in amplitude <50% from baseline	1	1	4.707	0.03004 *
	Fall in amplitude > 50% from baseline	20	1		

(Chi square test - * significant, NS – not significant at p value < 0.05)

18 out of 21 patients in Propofol group (Group P) developed change in NIHSS score >2 with corresponding fall in Cortical N19 amplitude of more than 50% on the tumor side at time interval T1 which was found to be statistically significant (p-0.0049). 20 out of 21 patients in Propofol group (Group P) developed change in NIHSS score>2 with corresponding fall in Cortical N19 amplitude of more than 50% on the tumor side at time interval T2 which was found to be statistically significant (p-0.03004). In contrast in Group D, zero and 1 patient at time interval T1 and T2 respectively, developed NIHSS score of >2 and corresponding fall in cortical N19 amplitude of more than 50%.(Table 10.1,10.2)

Table 11.1 Association of fall in N19 amplitude by >50% in Propofol group (Group P) with type of tumor (high grade glioma/low grade glioma):

Amplitude variation from baseline in Group P	High grade glioma (HGG)	Low grade glioma (LGG)	Chi square value	p value
<50% from the baseline	01	09	7.163	0.00744*
>50% from the baseline	19	01		

Table 11.2Association of fall in N19 amplitude >50% in Dexmedetomidine (Group D) with type of tumor (high grade glioma /low grade glioma):

Amplitude variation from baseline in Group D	High grade glioma (HGG)	Low grade glioma (LGG)	Chi square value	p value
<50% from the baseline	16	07	1.223	0.26877
>50% from the baseline	01	01		

19 out of 20 patients with high grade glioma and 1 patient out of 10 patients with low grade gliomas in Group P showed a fall in N19 amplitude of more than 50% from the baseline which was found to be statistically significant (p-0.00744). Therefore, the fall in N19 cortical response was more predominant in patients with diagnosis of high grade glioma in Group P. However, only one patient with high grade glioma and one patient with low grade glioma showed a fall in N19 amplitude of more than 50% in Group D from the baseline which was not found to be

statistically significant (p- 0.26877). Thus, it was noted that fall in cortical N19 response was predominantly seen in patients with high grade gliomas on sedation with Propofol.(Table 11.1,11.2)

Table 12.Association between NIHSS score and type of tumor:

	NIHSS SCORE	High grade glioma (HGG)	Low grade glioma (LGG)	Chi square	P value
GROUP P	**<2**	01	08	10.519	0.001181*
	>2	19	02		
GROUP D	**<2**	16	08	1.223	0.2687
	>2	01	01		

19 patients out of 22 with high grade gliomas and 3 patients out of 8 patients with low grade gliomas in Group P had NIHSS score change of more than 2 which was found to be statistically significant (p-0.001181). However, only 1 patient out of 17 patients with high grade glioma and 1 patient out of 8 patients with low grade glioma in Group D had NIHSS score change of more than 2 which was not found to be statistically significant (p-0.2687).(Table 12).

COMPLICATIONS OF THE ANESTHETIC REGIMEN

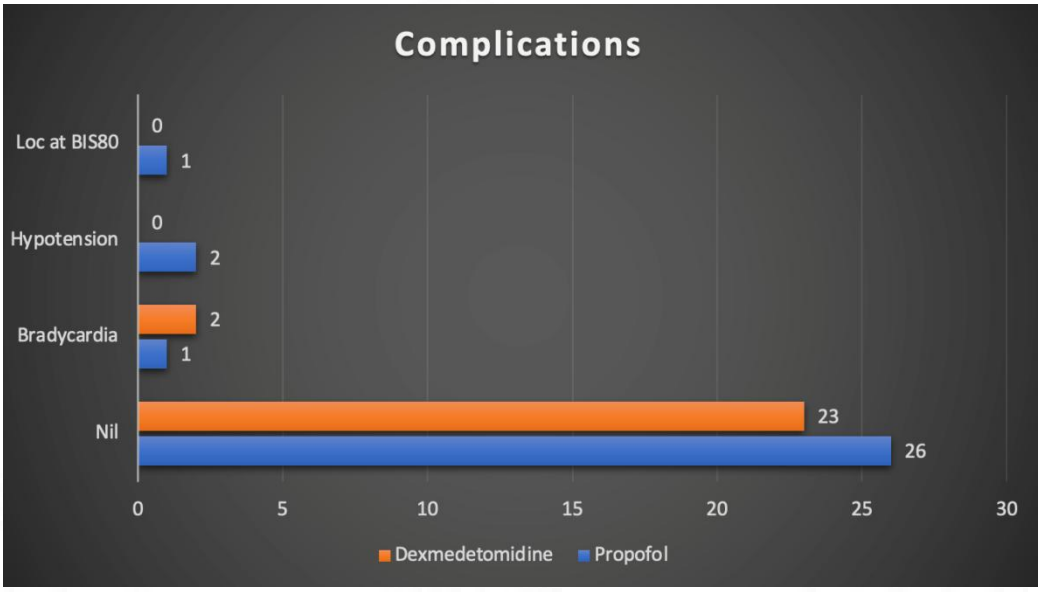


Fig 15. Complications of the Anesthetic Regimen

Table 13. Showing comparison of the adverse events during sedation procedure (elaborate)

Complications	Group P (n=30)		Group D(n=25)	
	Number	Percentage	Number	Percentage
Nil	26	86.6%	23	92%
Bradycardia	01	3.33%	02	8%
Hypotension	02	6.67%	00	0%
LOC at BIS of 80	01	3.33%	00	0%

Incidence of bradycardia was higher with Dexmedetomidine group compared to Propofol group (8% vs 3.33%). As shown in the table, incidence of sudden hypotension was seen in Propofol group which was easily treated with vasopressors. One patient developed sudden loss of consciousness due to large space occupying lesion in the dominant hemisphere who recovered within few minutes following termination of Propofol infusion.

Table 14.Association between post sedation and postoperative NIHSS scores at time interval (T3)

Group P	After sedation	Post-operative (T3)		Chi square	p value
		NIHSS>2	NIHSS<2		
NIHSS>2	21	10	11	1.22	0.54
NIHSS<2	8	2	6		

Group D	After sedation	Post-operative (T3)		Chi square	p value
		NIHSS>2	NIHSS<2		
NIHSS>2	2	1	1	0.091	0.955
NIHSS<2	23	9	14		

As shown in table 14, incidence of patient developing significant deficits with NIHSS >2 in postoperative period at time interval T3 was similar in both groups (40% in both the groups). In Propofol group (Group P) patients with NIHSS >2 following sedation had 50% incidence of developing post operative deficits . However, it was found to be statistically insignificant .

DISCUSSION

5. DISCUSSION

It has been postulated that certain anesthetic agents cause unmasking of focal neurological deficits in a particular cohort of patients with acute /subacute neurological dysfunction. The evidence for such effects by anesthetic agents is limited in the available literature. (29, 30, 31, 32) Moreover, this unmasking of deficits by the anesthetic agents has not been substantiated with corroborative electrophysiological evidence. Sedation is administered during various procedures in Neuroanesthesia practice, including awake craniotomy for neuromonitoring. This unmasking effect could be a serious concern when such patients undergo various procedures under sedation or general anesthesia.

Our study aimed to provide clinical and electrophysiological evidence of whether anesthetic agents can induce neurological deficits. In the current study, we have compared two agents acting on different brain regions to produce sedation, namely, Propofol and Dexmedetomidine. In our study, we found that at similar OASS scores and BIS values, a significant number of patients receiving Propofol was found to have unmasking of focal neurological deficits, as well as changes in amplitude of cortical (N19) SSEP potential. However, this unmasking was not seen in the patients receiving Dexmedetomidine. Moreover, we also noted that these findings were seen highest in patients with high grade glioma.

Our study was conducted preoperatively prior to induction of general anesthesia and surgery to negate the confounding factors affecting the study results. We compared two commonly used drugs for procedural sedation,i.e., Propofol and Dexmedetomidine. We have also compared hemodynamic stability and

complications between the two anesthetic regimens. We noted both the groups were comparable at baseline in terms of demographics, NIHSS score, and SSEP recording.

We recorded baseline NIHSS pre-operatively and included patients with NIHSS score of zero alone. NIHSS is a well established neurological assessment tool and used for the evaluation of acute stroke patients. This 15-item scale questionnaire showed high inter-rater reliability of kappa=0.69 and also has demonstrated good inter-rater reliability between neurologists and non-neurologists .(35,48)This scale helps to quantify neurological deficits and has good reproducibility.It has also been used in a study conducted by Nan Linn et al. to subjectively identify the worsening of neurological function .(32)

We have used bilateral median nerve SSEP, which is found to be highly specific for the detection of neurological deficits in spine surgeries. (49). In an extensive study of posterior fusion surgeries, significant changes in SSEP waveforms are associated with 13 times the odds of postoperative neurological deficits. (50). Another study evaluating the incidence of postoperative stroke in intracranial aneurysm surgery found that SSEP has Sensitivity and specificity were 42% and 90%. (51)

Median nerve SSEPs of the upper limb were recorded bilaterally at baseline before starting sedation designated as T0. The amplitude and latency of N9, P13, and N19 waveforms were recorded in bilateral upper limbs in a total of thirty patients in Group P and twenty five patients in Group D. The baseline values were comparable between the groups and were within normal limits bilaterally.

We achieved the target sedation levels based on an OASS score of 4 and between BIS of 60-80 in both groups at T1 and T2 time periods. In addition, after

starting sedation, the amplitude and latency of all wave forms,i.e., N9, P13, and N19, were recorded and compared at three time intervals –baseline(T0), after 10 minutes(T1), and after 15 minutes (T2) for the tumor vs. non tumor side along with corresponding NIHSS.

a) Changes in NIHSS

We observed that twenty one patients had an increase in NIHSS score of more than 2 from baseline when sedated with Propofol. NIHSS score change was significantly higher in patients receiving Propofol sedation with a mean score of 2.63±1.16 compared to the Dexmedetomidine group with a mean score change of 1.12±0.44. However, in the Dexmedetomidine group, only 2 out of 25 patients had a NIHSS score >2.The majority of score change was in limb motor function (40%), where the point score change ranges from score 0 to score 4, which indicates "normal" to "no movement" respectively, and ataxia (50%), where the points ranged from score 0 to score 1 which indicates "ataxia absent" and "ataxia present" respectively.10% of patients developed aphasia, 20% developed loss of orientation and 10% developed difficulty in articulation. Our results show that sedation with Propofol resulted in the unmasking of focal neurological deficits compared to Dexmedetomidine despite similar sedation scores.

b) Changes in SSEP:

We also noted that bilateral SSEP recordings of cortical and subcortical potentials showed different changes between the two groups and tumor and non-tumor hemispheres. There was no significant change between the two groups regarding the amplitude of cortical N19 and subcortical (N9 and P13) atT0, T1, and T2 intervals on the non-tumor side. The latency of cortical and subcortical potentials

was maintained in the Propofol group at T0, T1, and T2 on both tumor and non-tumor sides. However, in patients receiving Dexmedetomidine (Group D), we observed an increase in latency (approximately 5% change) of subcortical potentials, i.e., N9 and P13 on both tumor and non-tumor sides from baseline at T1 and T2 periods. Though this change was statistically significant, it was not clinically insignificant as per the described warning criteria of SSEP monitoring. (latency increase of more than 10% from the baseline).There was no significant change in latency of N19 potentials in the Dexmedetomidine group.

There was a significant fall in amplitude (>50%)of cortical potential (N19) at time intervals, T1 and T2 compared to baseline in patients receiving Propofol sedation (Group P) on the tumor side. This change was statistically significant and clinically relevant based on the warning criteria of SSEP (amplitude decrease of more than 50% from the baseline). Conversely, there was no change in amplitude of N19 potential in patients receiving Dexmedetomidine sedation.

The observed changes in SSEP could be due to the differential site of action of the two agents on the brain to produce sedation. Propofol acts on the cerebral cortex, whereas Dexmedetomidine causes its effects by acting on locus ceruleus.

On further analysis, we noted that 18 out of 21 patients who had changes in NIHSS >2 also showed a decrease in N19 cortical amplitude at T1 on the tumor side, and 20 of 21 patients who had a change in NIHSS score >2 also had a concomitant fall in N19 cortical amplitude on tumor side at time interval T2 which was found to be statistically significant. However, the Dexmedetomidine group did not show a similar correlation between NIHSS score changes and N19 cortical response (Group D).

The associated changes in NIHSS and N19 cortical amplitude response were found to occur predominantly in patients with high-grade gliomas compared to those with low-grade gliomas.

In our study, we recruited patients diagnosed with fronto-temporo-parietal gliomas. Gliomas are intra-axial tumors that usually infiltrate deep into white matter and disrupt functional integrity. However, this destruction of white matter is compensated by the dynamic re-organization of the neuronal circuit, which makes the clinical symptoms appear less severe as compared to its imaging.(52) Patients with gliomas in eloquent areas do not show any apparent deficits in formal clinical examination, but usually complain of fine motor dysfunction. Hence, we selected patients who had gliomas in eloquent areas of the brain to test for any potential motor/sensory deficits that could be unmasked, which we believed were more vulnerable to sedative agents.

Thal et al. conducted a study to compare unmasking of focal neurological deficits occurring due to fentanyl versus midazolam in 54 un premedicated patients with a brain tumor and carotid disease. This study relied heavily on detailed neurological examination involving mental state evaluation to detect any changes in neurological function from the baseline. It limited itself to examining motor system and reflexes, which are easy to quantify but highly objective. In our study, we conducted NIHSS for neurological examination and supported the findings with concomitant Somatosensory evoked potential examination.(30)

In a similar study, Nan Linn et al. hypothesized that the worsening of neurological function is a feature common to all sedatives. To accept this hypothesis, all anesthetic agents should produce worsening neurological function when

administered to patients at comparable levels of sedation. This was the first study on patients with supratentorial tumors, as all previous unmasking studies were conducted on patients with stroke or carotid disease. They conducted the study on 124 patients with supratentorial tumors, of which 90 patients had no baseline neurological deficits.They tested the effect of commonly used sedative agents,i.e., midazolam, fentanyl, Propofol, and Dexmedetomidine. The proportion of significant NIHSS change (NIHSS>2) was seen in case of midazolam -72%, Propofol – 52%, fentanyl -27% and Dexmedetomidine 23% ($p<0.01$among groups). This study proved that midazolam and Propofol cause unmasking of neurological deficits in greater frequency compared to fentanyl or Dexmedetomidine. This was in agreement with our study, which also found that the incidence of NIHSS positive change with Propofol was very high (71%) compared to the study by Linn et al., which was just 52%. Also, the incidence of Dexmedetomidine causing NIHSS positive change was significantly lower 4%, compared to 23%, as described by Linn et al.(33)

The component of NIHSS which was most affected was the limb motor weakness and ataxia, similar to our study. They concluded that patients with high-grade gliomas were more susceptible to induced neurological dysfunction, irrespective of the sedative. Our study found that Dexmedetomidine does not cause a significant change in NIHSS, even in patients with high-grade gliomas.

Also, we established corroborative evidence by performing a concomitant SSEP of the median nerve of bilateral upper limbs. Most patients,i.e., 18 of 21 at time interval T1 and 20 of 21 at time interval T2, had a change in NIHSS >2 and associated fall in N19 cortical SSEP response on the tumor side . This also proved

that NIHSS could be used as a clinical tool to detect the unmasking of focal deficits in resource-limited settings where SSEP is unavailable.

Linn et al. conducted yet another study on patients with supratentorial high-grade gliomas to further strengthen their findings.(53) He hypothesized that Midazolam sedation induces upper limb coordination deficits in patients with gliomas which can be reversed by flumazenil,a benzodiazepine antagonist. This study had a sample size of 32 patients, having 15 patients with glioma and 17 patients without glioma as the control group. Following midazolam administration, time to task completion was assessed by the time taken to complete 9 peg hole test (9PHT) performed both by the ipsilateral and the contralateral hand to the tumor side. The 9 peg hole test could quantify and accurately detect any deficits. According to the author, this test goes beyond the assessment of a single neurological function and tests hand-eye, motor coordination, and upper limb dexterity. It was found that the upper limb contralateral to the tumor performed poorly and took longer (26.5 seconds longer) than the baseline, which was statistically significant. This delayed performance was wholly reversed with the use of flumazenil. Our study did not use any complex clinical method like 9 peg hole test to determine the unmasking. We also did not check for the reversibility of Propofol /Dexmedetomidine as -1)The absence of Propofol or Dexmedetomidine antagonist which will successfully reverse the effect of the drug 2) We found it ethically inappropriate to reverse sedation precipitously before major resection surgery.

However, we also found that the motor deficits and ataxia were contralateral to the location of the tumor.This also established the role of GABAergic agents like Propofol and midazolam, which cause transient unmasking of neurological deficits.

A recent meta-analysis by Rizk et al. underlines the importance of these findings. They elucidated that unmasking of neurological deficits occurs primarily in two categories of patients- patients with brain mass lesion / acute or chronic infarction(54). Furthermore, several potential mechanisms have been put forth, which include:

1) Neurons present in the region of the previously injured brain are more vulnerable to these medications. Some theories suggest altered synaptic connectivity and change in pharmacodynamic processing of sedative medications. This has been evidenced by altered cerebral metabolism in the area of the pathological brain due to variation in local blood flow, increased uptake of the drug, slow washout, and liability to metabolic suppression .(30,32)
2) Studies conducted in patients with gliomas showed that due to extensive white matter infiltration, there is also differential cross hemispheric connections and a decrease in long-distance connectivity, which might explain patient presenting with a significant score change in high-grade gliomas like ataxia, limb incoordination, and sensory abnormalities rather than just localized deficits.(54)

Our study did not attempt to explain the pathological mechanism behind this unmasking. However, our study is the first to provide electrophysiological evidence of the mechanism of unmasking when all other studies tested unmasking using clinical examination, which is highly subjective and prone to bias.

Many studies have been conducted to determine the effects of Propofol and Dexmedetomidine on amplitude and latency of SSEP. Propofol, when used in sedative doses, has a negligible effect on subcortical waveforms and causes no change in cortical amplitude with <10% increase in latency.(19) However, in our

study, when Propofol was administered to patients with high-grade gliomas, patients had a fall in N19 cortical amplitude by more than 50% associated with unmasking of focal deficits. This might be due to the fact that both midazolam and Propofol act via GABAergic receptors at the cortical level. It also alters dopaminergic and serotonin activity. On the other hand,Dexmedetomidine acts specifically on locus coeruleus (i.e., acts subcortically) and hence did not significantly affect amplitude or latency.

We also compared the hemodynamic stability between the two anesthetic regimens. The incidence of bradycardia was higher in the Dexmedetomidine group following sedation compared to patients who received Propofol. We also noted that the mean arterial pressure of patients both in the Dexmedetomidine and Propofol group at time intervals T1 and T2 was lower compared to the baseline. However, patients who received Dexmedetomidine had lower mean arterial pressure thanthe Propofol group, which was statistically significant. These results were similar to Uddalaket al., who studied hemodynamic differences between Dexmedetomidine and Propofol and found that both heart rate and mean arterial pressure was lower in Group D as compared to group P. (55) In our study, even though there was a fall in mean arterial pressure in both groups compared to baseline it was not found to clinically significant. (<20%)

The baseline BIS values were comparable in both groups .Many studies have used depth of anesthesia monitor during Dexmedetomidine sedation and have found a good correlation with other scales like Observer assessment of Alertness/Sedation score .(34)

We noted that at an OASS score of 4, the Propofol group had a statistically significant fall in BIS value compared to the Dexmedetomidine group at both T1 and

T2 interval compared to baseline. However, NIHSS and SSEP was conducted only when all the patients had achieved a similar level of sedation,i.e., BIS value of 60-80 and OAA/S of 4

Our study also observed that the unmasking of neurological deficits was significantly greater in the subgroup of patients with high-grade glioma than in patients with low-grade gliomas.

This could be due to significant tissue destruction with more potential for white matter infiltration and faster growth of high-grade gliomas compared to slow-growing low-grade gliomas, which allow better functional compensation.

Our study results have broad implications. At present, there is increasing emphasis on continuous neurological monitoring in different clinical scenarios ranging from awake craniotomy, functional neurosurgery, sedation and wake-up tests in neurocritical care, monitored anesthesia care/sedation in patients interventional radiology like carotid stenting, balloon occlusion tests, mechanical thrombectomy for acute stroke. Our study shows that Dexmedetomidine sedation may be beneficial when clinical testing is employed in the above situations. Moreover, caution must be exercised if new onset neurological deficits are observed in patients on Propofol sedation.

Limitation of the study:

1) This study was conducted in a single center in 60 patients. A large multicenter trial may be required for better understand its clinical implications.
2) The use of Bi spectral index (BIS), which evaluates depth of anesthesia is based on processed EEG cannot be justified completely for depth of sedation monitoring in Dexmedetomidine based regimen. Hence, we supplemented it with Observer Assessment of Awareness/Sedation score which is a clinical scoring system and was comparable in both groups.
3) We did not check for the reversibility of the transient focal deficits that occurred following Propofol sedation. After the study was completed, we proceeded for general anesthesia for the neurosurgical procedure.
4) We did not attempt to pharmacologically antagonize or reverse drug induced changes on neurological examination as we believed it to be ethically inappropriate to reverse sedation precipitously in a patient undergoing major resection surgery.
5) We have not included patients with in other lobes or deep seated brain tumors or vascular lesions and infratentorial tumors. Hence, we cannot extrapolate our results to other conditions.

SUMMARY AND CONCLUSION

6. SUMMARY AND CONCLUSION

Propofol and Dexmedetomidine are commonly used drugs for procedural sedation. These are the commonly used as infusion to maintain sedation in patients where neurological testing is preferred. Based on the study of patients with frontotemporal gliomas, we concluded that;

1) Propofol can cause exaggeration or unmasking of focal neurological deficits especially in patients as determined by NIHSS and upper limb SSEP monitoring in patients with High grade glioma. This can potentially interfere with intraoperative clinical testing during resection and can confound the testing.
2) Dexmedetomidine has emerged as a viable alternative to Propofol sedation as it does not cause focal deficits and acts on subcortical level.
3) The changes in NIHSS correlated well with SSEP changes. Hence can be used as an alternative to electrophysiological test like SSEP in resource limited settings.

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ANNEXURES

PROFORMA

TITLE:

Comparison of effect of Propofol Vs Dexmedetomidine infusion on unmasking focal neurological deficits and Somatosensory evoked potential (SSEP) changes in Supratentorial brain tumor patients undergoing neurosurgery.

Sl NO: DATE:

AGE:

GENDER:M/F HEIGHT WEIGHT

DIAGNOSIS:

PREOPERATIVE COMPLAINTS:

PREOPERATIVE MRI/CT FINDINGS:

ASA GRADE:

DATE OF SURGERY:

BASELINE PARAMETERS:

HEART RATE: MAP: SPO2:

GROUP-P/D-

A.VITALS AND OASS SCORE

	BASELINE	POST SEDATION - 5 MIN	POST SEDATION- 10 MIN
HEART RATE			
BLOOD PRESSURE			
SPO2			
EtCO2			
RESPIRATORY RATE			
BIS			
OASS SCORE 5-ALERT 4-LETHARGIC 3-AROUSED BY VOICE 2-AROUSED BY SHAKING 1-DEEP SLEEP			

B. NIHSS SCORING

NIHSS SCORING		PRE OP	POST SEDATION-5MIN	POST SEDATION - 10 MIN
1A) LOC	0-ALERT 1DROWSY 2-OBTUNDED 3-COMA			
1B)ORIENTATION CURRENT MONTH/AGE	0-ANSWERS BOTH 1-ANSWERS1 2-ANSWERS NEITHER			
1C)RESPONDS TO COMMANDS	0-PERFORMS BOTH TASKS 1-ONE TASK PERFORMED 2-PERFORMS NEITHER			
2)GAZE	0-NORMAL 1-PARTIAL GAZE PALSY 2-COMPLETE GAZE PALSY			
3)VISUAL FIELDS	0-NO FIELD DEFECT 1-PARTIAL HEMIANOPIA 2-COMPLETE HEMIANOPIA 3-BILATERAL HEMIANOPIA			
4)FACIAL MOVEMENTS	0-NORMAL 1-MINOR FACIAL WEAKNESS 2-PARTIAL FACIAL			

	WEAKNESS 3-COMPLETE U/L PALSY			
5)MOTOR FUNCTION (ARM) A)LEFT B)RIGHT	0-NO DRIFT 1-DRIFT BEFORE 5 SEC 2-FALLS BEFORE 10S 3-NO EFFORT AGAINST GRAVITY 4-NO MOVEMENT			
6)MOTOR FUNCTION (LEGS) A)LEFT B)RIGHT	0-NO DRIFT 1-DRIFT BEFORE 5 S 2-FALLS BEFORE 10 S 3-NO EFFORT 4-NO MOVEMENT			
7)LIMB ATAXIA	0-NO ATAXIA 1-ATAXIA IN ONE LIMB 2-ATAXIA IN 2 LIMBS			
8)SENSORY	0-NO SENSORY 1-MILD SENSORY LOSS 2- SEVERE SENSORY LOSS			
9)LANGUAGE	0-NORMAL 1-MILD APHASIA 2-SEVERE APHASIA 3-MUTE/GLOBAL APHASIA			
10)ARTICULATION	0-NORMAL 1-MILD			

	2-SEVERE			
11)INATTENTION	0-ABSENT 1-MILD 2-SEVERE			

C.SOMATOSENSORY EVOKED POTENTIAL:

	RIGHT UPPER LIMB				LEFT UPPER LIMB			
	AMPLITUDE (P13)	LATENCY(P13)	AMPLITUDE(N22)	LATENCY(N22)	AMPLITUDE(P13)	LATENCY(P13)	AMPLITUDE(N22)	LATENCY(N22)
BASE LINE								
POST SEDATION								
5MIN								
10 MIN								

E.COMPLICATIONS IF ANY:

F. INTERVENTION : NEEDED/NOT NEEDED.

G.POST OP NEUROLOGICAL DEFICITS-

NAME AND SIGNATURE OF THE INVESTIGATOR (with date):

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

Time: ___ ___:___ ___ [ ]am [ ]pm

Person Administering Scale _____

Administer stroke scale items in the order listed. Record performance in each category after each subscale exam. Do not go back and change scores. Follow directions provided for each exam technique. Scores should reflect what the patient does, not what the clinician thinks the patient can do. The clinician should record answers while administering the exam and work quickly. Except where indicated, the patient should not be coached (i.e., repeated requests to patient to make a special effort).

Instructions	Scale Definition	Score
1a. Level of Consciousness: The investigator must choose a response if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.	0 = **Alert;** keenly responsive. 1 = **Not alert**; but arousable by minor stimulation to obey, answer, or respond. 2 = **Not alert**; requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped). 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and areflexic.	_____
1b. LOC Questions: The patient is asked the month and his/her age. The answer must be correct - there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues.	0 = **Answers** both questions correctly. 1 = **Answers** one question correctly. 2 = **Answers** neither question correctly.	_____
1c. LOC Commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him or her (pantomime), and the result scored (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored.	0 = **Performs** both tasks correctly. 1 = **Performs** one task correctly. 2 = **Performs** neither task correctly.	_____
2. Best Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored, but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI), score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements, and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.	0 = **Normal.** 1 = **Partial gaze palsy;** gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present. 2 = **Forced deviation,** or total gaze paresis not overcome by the oculocephalic maneuver.	_____

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat, as appropriate. Patients may be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia, is found. If patient is blind from any cause, score 3. Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a 1, and the results are used to respond to item 11.	0 = **No visual loss.** 1 = **Partial hemianopia.** 2 = **Complete hemianopia.** 3 = **Bilateral hemianopia** (blind including cortical blindness).	_____
4. Facial Palsy: Ask – or use pantomime to encourage – the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barriers obscure the face, these should be removed to the extent possible.	0 = **Normal** symmetrical movements. 1 = **Minor paralysis** (flattened nasolabial fold, asymmetry on smiling). 2 = **Partial paralysis** (total or near-total paralysis of lower face). 3 = **Complete paralysis** of one or both sides (absence of facial movement in the upper and lower face).	_____
5. Motor Arm: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine). Drift is scored if the arm falls before 10 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** limb holds 90 (or 45) degrees for full 10 seconds. 1 = **Drift;** limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 = **Some effort against gravity;** limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = **No effort against gravity;** limb falls. 4 = **No movement.** UN = **Amputation** or joint fusion, explain: _____ **5a. Left Arm** **5b. Right Arm**	_____ _____
6. Motor Leg: The limb is placed in the appropriate position: hold the leg at 30 degrees (always tested supine). Drift is scored if the leg falls before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic leg. Only in the case of amputation or joint fusion at the hip, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** leg holds 30-degree position for full 5 seconds. 1 = **Drift;** leg falls by the end of the 5-second period but does not hit bed. 2 = **Some effort against gravity;** leg falls to bed by 5 seconds, but has some effort against gravity. 3 = **No effort against gravity;** leg falls to bed immediately. 4 = **No movement.** UN = **Amputation** or joint fusion, explain: _____ **6a. Left Leg** **6b. Right Leg**	_____

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days [ ] 3 months [ ] Other _____(___ ___)

		_____
7. Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice. In case of blindness, test by having the patient touch nose from extended arm position.	0 = **Absent.** 1 = **Present in one limb.** 2 = **Present in two limbs.** UN = **Amputation** or joint fusion, explain: _____	_____
8. Sensory: Sensation or grimace to pinprick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for hemisensory loss. A score of 2, "severe or total sensory loss," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will, therefore, probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (item 1a=3) are automatically given a 2 on this item.	0 = **Normal;** no sensory loss. 1 = **Mild-to-moderate sensory loss;** patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched. 2 = **Severe to total sensory loss;** patient is not aware of being touched in the face, arm, and leg.	_____
9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For this scale item, the patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet and to read from the attached list of sentences. Comprehension is judged from responses here, as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in a coma (item 1a=3) will automatically score 3 on this item. The examiner must choose a score for the patient with stupor or limited cooperation, but a score of 3 should be used only if the patient is mute and follows no one-step commands.	0 = **No aphasia;** normal. 1 = **Mild-to-moderate aphasia;** some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response. 2 = **Severe aphasia;** all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = **Mute, global aphasia;** no usable speech or auditory comprehension.	_____
10. Dysarthria: If patient is thought to be normal, an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barriers to producing speech, the examiner should record the score as untestable (UN), and clearly write an explanation for this choice. Do not tell the patient why he or she is being tested.	0 = **Normal.** 1 = **Mild-to-moderate dysarthria;** patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = **Severe dysarthria;** patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. UN = **Intubated** or other physical barrier, explain:_____	_____

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

11. Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.	0 = **No abnormality.** 1 = **Visual, tactile, auditory, spatial, or personal inattention** or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = **Profound hemi-inattention or extinction to more than one modality;** does not recognize own hand or orients to only one side of space.	_____

_____

_____

CONSENT FORM

Title: Comparison of effect of Propofol vs Dexmedetomidine infusion on unmasking the focal neurological deficits and ssep changes in supratentorial brain tumour patients undergoing neurosurgery.

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 comparison of effect of Propofol vs Dexmedetomidine infusion on unmasking the focal neurological deficits and SSEP changes in supratentorial brain tumour patients undergoing neurosurgery. ( )
- 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

ന്യൂറോശസ്ത്രക്രിയയ്ക്ക് വിധേയരാകുന്ന തലച്ചോറിലെ സൂപ്രാടെന്റോറിയത്തിലെ മുഴയുള്ള രോഗികളുടെ മുഖത്ത് പ്രകടമാകുന്ന ന്യൂറോളജിക്കലായ പോരായ്മകളിലും എസ്എസ്ഇപി വ്യത്യാസങ്ങളിലും, പ്രൊപ്പഫോളിന്റെയും ഡെക്സ്മെഡിറ്റോമിഡിന്റെയും പ്രഭാവങ്ങൾ തമ്മിലുള്ള താരതമ്യം

പഠനത്തിൽ പങ്കെടുക്കുന്നയാളുടെ പേര് ....

ജനനതീയതി/വയസ്സ് ... . മാസങ്ങളിൽ/വർഷത്തിൽ

ഞാൻ.....മകൻ/മകൾ.....

(പ്രസക്തമായ കോളങ്ങളിൽ ശരിയടയാളമിടുക)

- എനിക്കു മുകളിൽ തന്ന ന്യൂറോശസ്ത്രക്രിയയ്ക്ക് വിധേയരാകുന്ന തലച്ചോറിലെ സൂപ്രാടെന്റോറിയത്തിലെ മുഴയുള്ള രോഗികളുടെ മുഖത്ത് പ്രകടമാകുന്ന ന്യൂറോളജിക്കലായ പോരായ്മകളിലും എസ്എസ്ഇപി വ്യത്യാസങ്ങളിലും, പ്രൊപ്പഫോളിന്റെയും ഡെക്സ്മെഡിറ്റോമിഡിന്റെയും പ്രഭാവങ്ങൾ തമ്മിലുള്ള താരതമ്യം എന്ന പഠനത്തിന്റെ കാര്യവിവരണപത്രം വായിച്ചു [ ]
- എനിക്കുണ്ടായ സംശയങ്ങൾ പരിഹരിച്ചു [ ]
- എന്റെ പങ്കാളിത്തം സ്വമേധയായാണെന്നും, എന്റെ പതിവ് ചികിത്സയെയോ നിയമപരമായ അവകാശങ്ങളോയോ ബാധിക്കാതെ ഏതു സമയത്തും പങ്കെടുക്കുനതിനുള്ള എന്റെ അനുവാദം പിൻവലിക്കാമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- പഠനത്തിൽനിന്നും ഞാൻ പിൻമാറിയാലും ഈ പഠനവുമായി ബന്ധപ്പെട്ട ആരോഗ്യരേഖകൾ പഠനസംഘംത്തിനും നൈതീക കമ്മിറ്റി അംഗങ്ങൾക്കും എന്റെ അനുവാദം കൂടാതെ പരിശോധിക്കാമെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. അതിന് ഞാൻ സമ്മതിക്കുന്നു. [ ]
- എന്റെ വ്യക്തിപരമായവിവരങ്ങൾ മുന്നാം കക്ഷികൾക്കോ പ്രസിദ്ധികരണത്തിനോ നൽകില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- പഠനത്തെപ്പറ്റിയോ പങ്കെടുക്കുന്നവരുടെ അവകാശത്തെപ്പറ്റിയോ കൂടുതലറിയണമെങ്കിൽ എനിക്ക് ബന്ധപ്പെടാനുള്ള നമ്പരുകൾ നൽകിയിട്ടുണ്ട്[ ]
- ഞാൻ സ്വമേധയാ ഈ പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിക്കുന്നു. [ ]
- 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

പ്രധാന ഗവേഷക

PATIENT INFORMATION FORM

TITLE: Comparison of effect of Propofol Vs Dexmedetomidine infusion on unmasking focal neurological deficits and Somatosensory evoked potential(SSEP) changes in patients with supratentorial brain tumour patients undergoing neurosurgery.

Name of the Investigators:

Dr.Sapna Suresh(PI), Dr.Manikandan S (Guide and CO-PI), Dr.Unnikrishnan.P.(Co guide and CO-PI),DrEaswer H.V (Co-investigator).

You are being requested to participate in the above titled study which is being conducted to evaluate theeffect of sedation by two commonly used drugs in neuroanesthesia ie, Propofol vs Dexmedetomidine on SSEP and on causing focal neurological deficits.We have planned to recruit60 people with supratentorial tumours –high grade gliomas posted for elective neurosurgical procedure at SCTIMST, Trivandrum.

What is NIHSS scoring?

It is a questionnaire scale employed by clinicians to assess neurological function. In this test the patient is asked to perform a few tasks like answer few questions, move limbs against gravity, read few lines etc,. This scale is made of 11 different elements that evaluate specific abilities. The score for each ability is given 0-4 score.This will be conducted before and after giving the test drug and requires maximum cooperation.

What is somatosensory evoked potential?

It is anon-invasive measurement of conduction of nerve signals to the brain. Stimulating electrodes will be placed over various nerves,such as ankle and wrist using a nerve stimulator and recording electrode are placed over sensory region of the brain. A small current will be given to the nerves which might cause slight discomfort and the recording electrode are placed over the scalp near the area where sensations are processed in the brain.

What happens during a SSEP testing?

The SSEP procedure itself is safe and non invasive.

1)Some detection electrodes will be glued to particular spots on your scalp and near the wrist.

2)A small generator is used to create tiny electrical impulse that will stimulate nerves at the wrist. While the impulses are usually not painful they will your thumb to twitch a little,which is normal.

3)In order for test to be accurate, it is important to listen carefully to person performing the test and try and relax.

4)Responseto electrical stimulus are recorded through the electrodes using special equipment.

What is BIS /BISPECTRAL INDEX?

BIS device consists of an adhesive electrode strip like a sticker placed on patient's forehead. The other end of the device will be connected to a monitor.This is used to monitor depth of sedation after giving the drug to the patient.

If you take part what will you have to do?

Preoperatively,NIHSS scoring will be undertaken and maximum score allotted. On the day of surgery, you will be taken inside the neuro Operation Theatre. All routine non invasive monitors to check your heart beat, blood pressure and oxygen saturation level will be attached. A 18G venous cannula will be inserted under local anaesthesia in the hand for fluid and drug administration which is routine in all patients. Baseline vitals will be recorded as per protocol.Sedation will be given to you to put you to light sleep. SSEP electrodes will be placed and after 5 and 10 min interval the level of sedation will be assessed following which NIHSS scoring and SSEP will be recorded

.

Does SSEP OR BIS monitoring have any side effects?

All these procedures are non-invasiveand routinely used to monitor patients. They don't carry any risk . Adverse events from doing these procedure is nil.

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.SAPNA SURESH(Principal investigator) mobile number: 8086177209. Email: sapna.gogi@gmail.com

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

രോഗികൾക്കുള്ള കാര്യവിവരണപത്രം

ശീർഷകം: ന്യൂറോശസ്ത്രക്രിയയ്ക്ക് വിധേയരാകുന്ന തലച്ചോറിലെ സൂപ്രാടെന്റോറിയത്തിലെ മുഴയുള്ള രോഗികളുടെ മുഖത്ത് പ്രകടമാകുന്ന ന്യൂറോളജിക്കലായ പോരായ്മകളിലും എസ്എസ്ഇപി വ്യത്യാസങ്ങളിലും, പ്രൊപ്പഫോളിന്റെയും ഡെക്സ്മെഡിറ്റോമിഡിന്റെയും പ്രഭാവങ്ങൾ തമ്മിലുള്ള താരതമ്യം

ഗവേഷകരുടെ പേര്:

ഡോ. സപ്ന സുരേഷ് (പ്രധാന ഗവേഷക), ഡോ. മണികണ്ഠൻ എസ് (ഗൈഡും സഹ പ്രധാന ഗവേഷകനും), ഡോ. ഉണ്ണികൃഷ്ണൻ പി (സഹഗൈഡും സഹപ്രധാനഗവേഷകനും)

പ്രൊപ്പഫോൾ ഡെക്സ്മെഡിറ്റോമിഡിൻ എന്നീ രണ്ട് മരുന്നുകൾ മയക്കാനുപയോഗിക്കുന്നതുകൊണ്ട് എസ്എസ്ഇപിയിലും മുഖത്തെ ന്യൂറോളജിക്കലായ പോരായ്മകളിലും ഉണ്ടാകുന്ന സ്വാധീനം വിലയിരുത്തുന്ന മുകളിൽ നൽകിയ ശീർഷകത്തിലുള്ള പഠനത്തിൽ പങ്കെടുക്കാൻ താങ്കളോട് അഭ്യർത്ഥിക്കുന്നു. സൂപ്രാടെന്റോറിയൽ മുഴകൾ- ഉയർന്ന തരം ഗ്ലിയോമയുള്ള, തിരുവനന്തപുരം, SCTIMST യിൽ നിശ്ചിതമായ ശസ്ത്രക്രിയയ്ക്ക് തീരുമാനിക്കപ്പെട്ട 60 രോഗികളെ ഉൾപ്പെടുത്താൻ ഞങ്ങൾ ആസൂത്രണം ചെയ്യുന്നു.

എൻഐഎച്ച്എസ് സ്കോറിംഗ് എന്നാലെന്ത്?
രോഗികളോട് ചില ചോദ്യങ്ങൾക്കുത്തരം നൽകാനും, കൈകാലുകൾ ഗുരുത്വാകർഷണത്തിനെതിരെ ചലിപ്പിക്കാനും, കുറച്ച് വരികൾ വായിക്കാനും പോലുള്ള ചില പ്രവർത്തികൾ ചെയ്യാൻ ആവശ്യപ്പെടുന്ന ചികിത്സകർ ഉപയോഗിക്കുന്ന ഒരു ചോദ്യാവലിയാണ് എൻഐഎച്ച്എസ്. (**NIHS**). പ്രത്യേക ശ്ഷികൾ വിലയിരുത്തുന്ന 11 ഘടകങ്ങൾ കൊണ്ടാണ് ഈ സ്കെയിൽ ഉണ്ടാക്കിയിരിക്കുന്നത്. ഓരോ ശ്ഷിക്കും 0 മുതല്ു 4 വരെ സ്കോറാണ് നൽകിയിരിക്കുന്നത്. പരീക്ഷണ മരുന്ന് നൽകുന്നതിനുമുമ്പും ശേഷവും ഈ പരിശോധന നടത്തും, രോഗിയുടെ പരമാവധി സഹകരണം ഇതിനാവശ്യമാണ്.

ശരീരത്തിലെ ഇന്ദ്രിയസംബന്ധിയായ അന്തർലീനശക്തി പ്രചോദിപ്പിക്കലെന്നാലെന്താണ്?
ശരീരത്തിൽ പ്രവേശിക്കാതെയുള്ള തലച്ചോറിലേയ്ക്കുള്ള നാഡീ സംജ്ഞകളുടെ പ്രവാഹം അളക്കുന്ന ഒന്നാണത്. കൈകാൽമുട്ടുകൾ, മണിബന്ധം തുടങ്ങിയ വിവിധ നാഡികളിൽ പ്രചോദനമുണ്ടാക്കുന്ന ഇലക്ട്രോഡുകളും തലച്ചോറിന്റെ ഇന്ദ്രിയ സംബന്ധമായ മേഖലകളിൽ രോഖപ്പെടുത്തുന്ന ഇലക്ട്രോഡുകളും ഘടിപ്പിക്കുന്നു. ചെറിയ അസ്വസ്ഥതയുണ്ടാക്കിയേക്കാവുന്ന ലഘുവായ വൈദ്യുതി നാഡികൾക്ക് നൽകി തലച്ചോറിന്റെ ഇന്ദ്രിയ സംബന്ധമായ മേഖലകളിൽ വച്ചിരിക്കുന്ന ഇലക്ട്രോഡുകളിൽ സംഞ്ജകൾ രേഖപ്പെടുത്തുന്നു.

എസ്എസ്ഇപി പരിശോധനയിൽ എന്തു സംഭവിക്കുന്നു?

എസ്എസ്ഇപി പരിശോധന ശരീരത്തിൽപ്രവേശിക്കാതെയുള്ളതും സുരക്ഷിതവുമാണ്.

1. തലയോട്ടിയിലെ പ്രത്യേക സ്ഥലങ്ങളിൽ ചില തിരിച്ചറിയൽ ിലക്ട്രോഡുകൾ ഒട്ടിച്ചുവയ്ക്കുന്നു.
2. ഒരു ചെറിയ ജനറേറ്റർ ഉപയോഗിച്ച് സൂക്ഷമമായ വൈദ്യുത പ്രേരണകൾ നൽകുകയും അവ മണികണ്ഠത്തിലെ നാഡികളെ പ്രചോദിപ്പിക്കുകയും ചെയ്യും., താങ്കളുടെ തള്ളവിരൽ ചെറുതായി വിറപ്പിക്കുന്ന- അത് സ്വാഭാവികമാണ്, പ്രേരണകൾ സാധാരണ വേദനാജനകമല്ല.
3. പരിശോധന കൃത്യമാകാൻ പരിശോധന നടത്തുന്നയാൾ പറയുന്നത് ശ്രദ്ധാപൂർവ്വം കേൾക്കുകയുംപിരിമുറുക്കം കുറയ്ക്കാൻ ശ്രമിക്കുകയും വേണം.
4. വൈദ്യുത പ്രേരണകളോടുള്ള പ്രതികരണം ഇക്ട്രോഡുകളിൽനിന്നും പ്രത്യേക ഉപകരണമുപയോഗിച്ച് രേഖപ്പെടുത്തും.

ബിസ്/ബൈസെപ്റ്റൽ ഇൻഡക്സ് എന്നാലെന്ത്?

ബിസ് ഉപകരണത്തിൽ രോഗിയുടെ നെറ്റിയിൽ വയ്ക്കുന്ന സ്റ്റിക്കർ പോലുള്ള ഒട്ടുന്ന ഒരു ഇലക്ട്രോഡുണ്ട്. ഉപകരണത്തിന്റെ മറ്റേയറ്റം ഒരു മോണിറ്ററുമായി ഘടിപ്പിക്കും. ഇത് രോഗിക്ക് മരുന്നു നൽകിയ ശേഷമുള്ള മയക്കത്തിന്റെ ആഴം നിരീക്ഷിക്കാൻ ഉപയോഗിക്കുന്നു.

താങ്കൾ പങ്കെടുക്കുകയാണെങ്കിൽ എന്തു ചെയ്യണം?

കസ്ത്രക്രിയയ്ക്കുമുമ്പ് എൻഐഎച്എസ് സേകോർ എടുക്കുകയും പരമാവധി സ്കോർ നൽകുകയും ചെയ്യും. ശസ്ത്രക്രിയാ ദിവസം താങ്കലെ ശസ്ത്രക്രിയാമുറിയിൽ പ്രവേശിപ്പിക്കും. താങ്കലുടെ ഹൃദയസ്പന്ദനം, രക്തസമ്മർദ്ദം, പ്രാണവായിവിന്റെ സമ്പുഷ്ടത എന്നിവ ശരീരത്തിൽ പ്രവേശിക്കാതെ നിരീക്ഷിക്കുന്ന ഉപകരണങ്ങൾ ഘടിപ്പിക്കും. ദ്രാവകങ്ങളും മരുന്നും നൽകാനായി കൈയിൽ പ്രാദേശികമായി മരവിപ്പിച്ച് ഒരു 18ജി കുഴൽ കടത്തും. നടപടിക്രമപ്രകാരം ജീവനപരമായ അടിസ്ഥാനങ്ങൾ രേഖപ്പെടുത്തും. താങ്കൽക്ക് മയക്കാനുള്ല മരുന്നു നൽകിയശേഷം എസ്എസ്ഇപി ഇലക്ട്രോഡികൾ സ്ഥാപിക്കുകയും അതിനുശേഷം 5 -10 മിനിട്ടുകളുടെ ഇടവേളകളിൽ മയക്കത്തിന്റെ നിലവാരം വിലയിരുത്തുകയും ശേഷം എൻഐഎച്എസ്എസ് സ്കോറിംഗും എസ്എസ്ഇപി സ്കോറിംഗും രേഖപ്പെടുത്തും.

എസ്എസ്ഇപി അല്ലെങ്കിൽ ബിസ് നിരീക്ഷണങ്ങൾക്ക് എന്തെങ്കിലും പാർശ്വഫലങ്ങളുണ്ടോ?

ഈ നടപടികളെല്ലാം ശരിരത്തിൽ കടക്കാതെയുളളതും ഒരു അപായവുമുള്ളതുമല്ല. ഈ നടപടിക്രമങ്ങൾക്ക് ദോഷവശങ്ങൽ ഒന്നുമില്ല.

പഠനമാരംഭിച്ചശേഷംതാങ്കൾക്ക് പിൻമാറാനാകുമോ?

താങ്കളുടെ പഠനത്തിലെ പങ്കാളിത്തം തികച്ചും സ്വമേധയായുള്ളതും സമ്മതം പിൻവലിക്കാൻ ഏതുസമയത്തും താങ്കൾക്ക് സ്വാതന്ത്യമുള്ളതുമാണ്. താങ്കളങ്ങനെ ചെയ്താലും ഈ ആശുപത്രിയിലെ താങ്കളുടെ പതിവ്ചികിത്സയെ ഒരുതരത്തിലും ബാധിക്കില്ല. തന്നെയുമല്ല, താങ്കൾക്ക് എന്തെങ്കിലും പാർശ്വഫലങ്ങൾ ഉണ്ടാവുകയാണെങ്കിൽ പഠനം നിർത്തുകയും പാർശ്വഫലങ്ങൾക്ക് ചികിത്സ നൽകുകയും ചെയ്യും.

ഈ പരിശോധനയ്ക്ക്താങ്കൾ പണം നൽകണോ?

ഇവ ശസ്ത്രക്രിയയിൽ മയക്കൽ നടപടികൾക്കുപയോഗിക്കുന്നവയാണ്, ആകയാൽ അധികമായി ഒരുചിലവും ഉണ്ടാകില്ല.

താങ്കളുടെവ്യക്തിപരമായവിവരങ്ങൾരഹസ്യമായിരിക്കുമോ?

താങ്കളുടെ വ്യക്തിപരമായ വിവരങ്ങൾ രഹസ്യമായിരിക്കും. ഈ പഠന ഫലങ്ങൾ അക്കാദമിക് ഗവേഷണത്തിന്റെ ഭാഗമായി ഉപയോഗിക്കുകയും ഒരുവൈദ്യശാസ്ത്ര ജേർണലിൽ പ്രസിദ്ധീകരണത്തിനയക്കുകയും ചെയ്യും. പക്ഷേ താങ്കളെ പേരുകൊണ്ട് പ്രസിദ്ധീകരണത്തിലോ പ്രദർശനത്തിലോ ഒരിടത്തും തിരിച്ചറിയാനാകില്ല. എന്നിരുന്നാലും, താങ്കൾ പഠനത്തിൽ പങ്കെടുക്കാൻ തീരുമാനിച്ചാൽ താങ്കളുടെ ചികിത്സാരേഖകൾ പഠനവുമായി ബന്ധപ്പെട്ടവർ താങ്കളുടെ വീണ്ടുമുള്ള സമ്മതമില്ലാതെ അവലോകനം ചെയ്തേക്കാം.

താങ്കൾക്ക് കൂടുതൽ ചോദ്യങ്ങളുണ്ടെങ്കിൽ ദയവായി ചോദിക്കുക, ഡോ. സപ്ന സുരോഷ് (പ്രധാന ഗവേഷക) മൊബൈൽ നമ്പർ 8086177209 ഇമെയിൽ sapna.gogi@gmail.com

പഠനത്തിന്റെ നൈതീക അനുവാദവുമായി ബന്ധപ്പെട്ട വിശദീകരണങ്ങൾക്ക് ഡോ. മാലാ രാമനാഥൻ, മെമ്പർ സെക്രട്ടറി, SCTIMST *IEC*, അഡീഷണൽ പ്രൊഫസർ/ ഫോൺ 2524234 ഇമെയിൽ iec.mem.sec@sctimst.ac.in

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/1566/OCTOBER-2020 30.11.2020

Dr. Sapna Suresh
Resident
Department of Anaesthesiology
SCTIMST, Thiruvananthapuram

Dear Dr. Sapna Suresh,

Thank you for submitting documents related to your proposal titled "**COMPARISON OF EFFECT OF PROPOFOL VS DEXMEDETOMIDINE INFUSION ON UNMASKING FOCAL NEUROLOGICAL DEFICITS AND CAUSING SSEP CHANGES IN SUPRATENTORIAL BRAIN TUMOR PATIENTS UNDERGOING NEUROSURGERY** (IEC/1566)" to the IEC for review.

The following documents were reviewed:

Original submission

1. *Checklist*
2. *Covering letter addressed to Chairman dated 14/08/2020 endorsed by HOD*
3. *TAC approval dated 27/07/2020 with comments and responses*
4. *IEC application form signed by PI*
5. *Study proposal*
6. *Proforma*
7. *Consent form (English)*
8. *Person obtaining consent certification*
9. *Consent form in Malayalam*
10. *Patient Information Sheet in English*
11. *Patient information sheet in Malayalam*
12. *Signed CV PI Dr. Sapna Suresh of TCMC Number dated 14.05.2020*
13. *Signed CV of Co-PI Dr.Manikandan with TCMC Number dated 26.06.2019*
14. *Signed CV of Co-PI Dr.Unnikrishnan with TCMC Number dated 04.05.2020*
15. *Signed CV of Co-PI Dr.Easwer with TCMC Number dated 04.02.2019*

Revised submission on 21/11/2020

1. *List of changes made in the submission in submission as per feedback*
2. *Covering letter addressed to Chairman dated 14/08/2020 endorsed by HOD*
3. *TAC approval dated 27/07/2020 with comments and responses*
4. *Revised IEC application form*
5. *Study proposal*
6. *Revised proforma*
7. *Consent form in English*
8. *Person obtaining consent in English*
9. *Consent form in Malayalam*
10. *Person obtaining consent in Malayalam*
11. *Revised patient information form in English*
12. *Revised patient information form in Malayalam*
13. *Signed CV PI Dr. Sapna Suresh of TCMC Number dated 14.05.2020*
14. *Signed CV of Co-PI Dr.Manikandan with TCMC Number dated 26.06.2019*
15. *Signed CV of Co-PI Dr.Unnikrishnan with TCMC Number dated 04.05.2020*
16. *Signed CV of Co-PI Dr.Easwer with TCMC Number dated 04.02.2019*

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

Technical Advisory Committee (Clinical Studies)

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

TAC Registration No: SCT-/S/2020/1096 **Date: 27.07.2020**

Project title: COMPARISON OF EFFECT OF PROPOFOL VS DEXMEDETOMIDINE INFUSION ON UNMASKING FOCAL NEUROLOGICAL DEFICITS AND CAUSING SSEP CHANGES IN SUPRATENTORIAL BRAIN TUMOR PATIENTS UNDERGOING NEUROSURGERY

Principal Investigator:
Dr Sapna Suresh, 1st st Year Resident, Division of NeuroAnaesthesia and Neurocritical care, Department of Anaesthesiology, SCTIMST Degree: DM (Neuroanesthesia)
Co-Principal Investigator(s):
Dr Manikandan S, Professor and Incharge, Division of NeuroAnaesthesia and Neurocritical care Department of Anaesthesiology, SCTIMST Degree: M.D., P.D.C.C.(Neuroanesthesia)
Dr.Unnikrishnan. P, Assistant Professor, Division of NeuroAnaesthesia and Neurocritical care Department of Anaesthesiology, SCTIMST Degree: M.D.,P.D.C.C..(Neuroanesthesia)
Dr Easwer HV, Professor, Department of Neurosurgery, SCTIMST Degree: MBBS, Mch (Neurosurgery)

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).

Appendix-1

The theoretical basis of this study is that the presence of possible secondary pathways that accomplish the function of destroyed neurons which are functional only in awake state and are unmasked when there is residual sedation as described "Diffrential awakening" by Cucchiara. This effect of anesthetic drugs is due to a non specific central effect unrelated to the specific effects of sedative drugs. The duration of this differential awakening was as short as 2 hours described by Lazar et al. In other study involving 4 anesthetic drugs, (midazolam, fentanyl, propofol and Dexmedetomidine), Dexmedetomidine produced the least effect on unmasking neurological deficits. A probable GABAergic mechanism was also attributed to this effect. In this proposed study, investigators are planning to study the neuroplasticity/ or the clinical vulnerability in patients with suspected neuropathology using the concept of "pharmacological stress test to the brain" by the commonly used anesthetic drugs for conscious sedation, ie; Propofol and Dexmeditomedine. This study may be useful in identifying patients with limited cerebral reserve using conscious sedation. Moreover, the investigators are also planning to assess the neurodeficits more objectively using the SSEP monitoring in addition to the subjective assessment by NIHSS described in previous studies. But there are a few queries.

1. Please explain why double blinding is not opted in the study design?

Answer: A double blinded study would have been ideal but it will not be possible in our study for the following reasons:

i) Propofol is white coloured liquid and Dexmedetomidine is a clear liquid.

ii) Onset of time of drugs and method of administration of the drugs are vastly different FOR EXAMPLE- Propofol is to be administered in TCI pump and dexmedetomidine is to be given in form an infusion slow i.v with an infusor pump.

2. Why group D is not receiving Fentanyl infusion during the Anesthesia maintenance? Since Fentanyl is also studied for assessing "Differential awakening" by other previous researchers, intraoperative Anesthesia maintenance may be standardized

Answer: Fentanyl has been included as drug to be administered to group D during maintenance of anaesthesia, as suggested.

3. Remove the term "Sir" after Dr Manikandan S, Dr Unnikrishnan P, in the investigators column in the TAC application

Answer: The above mentioned changes have been made in TAC application form.

Ouriginal by Turnitin

Document Information

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Sources included in the report

W URL: https://pubs.asahq.org/anesthesiology/article/124/3/598/14288/Mild-Sedation-Exacerbates-or-Unmasks-Focal
Fetched: 2021-01-04 20:58:22 3

Entire Document

1.INTRODUCTION “Brain tumors” are a complex group of neoplasms arising from intracranial tissue and /or the meninges. The annual incidence of brain tumors (including primary brain tumors and lymphomas with the exclusion of spinal tumors) is around 7 per 100,000 population. (1)
Most intracranial tumors in adults arise from the supratentorial region (<80%). With the use of newer technologies such as neuro navigation and intraoperative mapping, the surgical goal aims to maximize the tumor resection while preventing any focal neurological deficits. Resection of infiltrative tumors located in eloquent areas of the brain has always been a neurosurgical challenge. Additionally, resection of infiltrative tumors without clear boundaries has resulted in a high incidence of permanent postoperative deficits (as high as 13- 17.9%). (2) Awake craniotomy has been considered beneficial in such tumors, as this enables cortical and sub cortical mapping and allows continuous neurological assessment of the patient.
Awake craniotomy presents the neuro anesthesiologist with a unique set of challenges. Choice of technique and medication varies institutionally, and the most common drugs used in the awake craniotomy are a combination of opioids like fentanyl, remifentanil, and sedation with either Propofol or Dexmedetomidine along with infiltration with local anesthetic agents. (3)
These sedative drugs ensure easy titratability, rapid onset and offset and facilitate intraoperative monitoring in awake patients. However, there have been recent reports of unmasking or exacerbation of focal neurological deficits in patients with tumors caused by sedative medication like midazolam, fentanyl , Propofol and, Dexmedetomidine as reported by Gary D et al. (4) Since these are the medications that are commonly used during awake craniotomy, concerns regarding them producing transient focal neurological deficits intraoperatively and potentially confounding neurological assessment is of grave concern. Also, to date, these studies have reported transient focal neurological deficits subjectively through assessment of these deficits with clinical examination. There is no literature on the objective evidence that the anesthetic agents will cause focal neurological deficits.Hence, we planned the current study to use a combination of clinical neurological testing and intraoperative evoked potential using somatosensory evoked potential (SSEP) to provide objective evidence to test if the sedative agents (Propofol and Dexmedetomidine) can cause focal neurological deficits in patients with supratentorial tumors.

sl.no	AGE	SEX	weight	Height	BMI	ASA	SIZE OF TUMOR	VOLUME OF TUMOR	MIDLINE SHIFT	PRE OPERATIVE COMPLAINTS	PRE OP STEROIDS	PRE OP NIHSS
	(in years)	(M/F)	(kgs)	(cms)	(kg/m2)	I/II	(CENTIMETRES)	(cm3)				
1	35	M	86	173	28.7	I	5.7X6.2X4.5	159.03	3mm	FOCAL SEIZURES,HEADACHE	dexamethasone	0
2	31	F	57	162	35.18	I	4.9X4.7X5.7	131.27	4mm	ACALCULIA,ALEXIA,ANOMIA	dexamethsone	0
3	45	M	64	169	22.45	II	3.3X3.2X3.2	33.79	3mm	HEADACHE	dexamethsone	0
4	36	F	45	162	17.17	I	4.5X4.4X6	118.8	5mm	HEADACHE	NO	0
5	39	F	60	163	22.65	I	5.9X3.3X3	58.41	5mm	FOCAL SEIZURES	dexamethasone	0
6	27	F	65	165	24.89	I	3.5X3X3.4	35.7	5mm	HEADACHE	NO	0
7	52	M	60	153	25.64	II	5.7X4.2X4.8	114.92	3mm	HEADACHE	dexamethasone	0
8	27	F	43	157	17.47	I	7.4X6.5X6.2	298.22	4mm	HEADACHE	NO	0
9	34	F	60	170	20.76	I	3.0X3.4X2.6	26.52	5mm	HEADACHE	dexamethasone	0
10	33	F	49.5	155	20.62	I	4.9X5.0X5.3	129.85	5mm	HEADACHE	dexamethasone	0
11	40	M	80	172	27.11	I	1.56X1.42X2.0	4.43	nil	HEADACHE,SEIZURE	NO	0
12	27	F	57	165	20.95	I	7.2X7.2X6.2	321.4	4mm	HEADACHE	dexamethasone	0
13	24	F	68	174	22.66	I	3.4X3.5X4.4	52.36	3mm	HEADACHE	dexamethasone	0
14	34	M	72	165	26.47	I	4.0x5.6x6.9	154.56	3mm	FOCAL SEIZURES	dexamethasone	0
15	34	F	48	149	21.62	I	3.0X5.0.3.0	45	5mm	HEADACHE ,SEIZURES	dexamethasone	0
16	27	F	74	170.5	25.6	I	4.0x5.6x6.9	154.56	5mm	HEADACHE	dexamethasone	0

sl.no	AGE	SEX	weight	Height	BMI	ASA	SIZE OF TUMOR	VOLUME OF TUMOR	MIDLINE SHIFT	PRE OPERATIVE COMPLAINTS	PRE OP STEROIDS	PRE OP NIHSS
17	47	M	52	156	21.3	II	3.0X4.0X2.0	24	3mm	HEADACHE	NO	0
18	46	F	62	156	25.5	II	4.0X3.0X4.0	48	4mm	HEADACHE ,SEIZURES	dexamethasone	0
19	40	M	80	175	26.2	II	3X3X2.0	18	4mm	SEIZURES	NO	0
20	33	F	55	160	21.5	I	4X5X3.0	60	5mm	HEADACHE,NAUSEA	dexamethasone	0
21	39	M	65	156	26.7	II	5.0X4.0X4.0	80	3mm	HEADACHE	dexamethasone	0
22	30	F	58	165	21.5	I	2X3X2.6	15.6	3mm	FOCAL SEIZURES	dexamethasone	0
23	48	M	73	170	25.4	II	4X5X3.0	60	5mm	FOCAL SEIZURES	dexamethasone	0
24	22	F	58	158	23.2	I	3X3X4.0	36	5mm	HEADACHE ,SEIZURES	dexamethasone	0
25	35	F	64	160	25.2	I	4X3X5.5	66	3mm	HEADACHE	dexamethasone	0
26	25	M	70	160	27.3	I	1.2X2X1.1	2.64	4mm	FOCAL SEIZURES	dexamethasone	0
27	27	F	60	152	26.66	I	3X4X4	48	6mm	HEADACHE	dexamethasone	0
28	30	M	70	155	29.1	II	4X3X5.5	66	7mm	HEADACHE ,SEIZURES	dexamethasone	0
29	45	F	70	165	25.73	II	4X3X4	48	8mm	HEADACHE	dexamethasone	0
30	34	F	75	170	25.95	II	3X5X5	75	6mm	HEADACHE ,SEIZURES	dexamethasone	0

sl.no	type of tumour(DIAGNOSIS)	CEREBRAL EDEMA	PROCEDURE	Heart rate (beats /minute)			MEAN BLOOD PRESSURE (MM OF HG	
	HGG/LGG	(Y/N)		baseline	AT T1	AT T2	BASELINE	AT T1
				T0	(after sedation)	(after sedation)	T0	after sedation
1	left frontotemporal glioma(HGG)	YES	left ftp craniotomy and excison	70	62	65	95	90
2	left parietal lobe(HGG)	YES	left ftp craniotomy and excison	80	77	66	75	76
3	left fronto parietal glioma (LGG)	YES	left frontotemporal craniotomy	76	66	65	85	87
4	left temporal glioma(LGG)	NO	left ftp craniotomy and excison	88	76	87	92	92
5	right temporal glioma(HGG)	YES	right ftp craniotomy and excision	85	76	67	85	80
6	left fronto parietal glioma (LGG)	NO	left ftp craniotomy and excison	80	75	70	90	89
7	right temporal glioma(HGG)	YES	right ftp craniotomy and excision	71	70	67	81	81
8	left frontal callosal lesion?glioma(HGG	YES	left frontotemporal craniotomy	84	75	78	94	78
9	left fronto parietal glioma (LGG)	NO	left frontotemporal craniotomy	87	76	61	96	90
10	right frontal glioma (HGG)	YES	right ftp craniotomy and excision	80	70	77	89	85
11	right frontotemporal glioma(LGG)	NO	right ftp craniotomy and excision	84	75	78	92	87
12	left parital lesion?(HGG)	YES	left ftp craniotomy and excison	80	70	77	94	81
13	left fronto parietal glioma (HGG)	YES	left ftp craniotomy and excison	85	75	70	94	89
14	right temporal glioma(HGG)	YES	right ftp craniotomy and excision	71	76	67	97	88
15	right parietal glioma(HGG)	YES	right ftp craniotomy and excision70	70	65	65	91	82
16	left fronto parietal glioma (HGG)	YES	left frontotemporal craniotomy	84	70	65	96	90

sl.no	type of tumour(DIAGNOSIS)	CEREBRAL EDEMA	PROCEDURE	Heart rate (beats /minute)			MEAN BLOOD PRESSURE (MM OF HG	
17	right frontotemporal glioma(LGG)	YES	right ftp craniotomy and excision	68	55	60	95	80
18	left fronto parietal glioma (LGG)	NO	left frontotemporal craniotomy	92	83	78	91	82
19	left temporal glioma (HGG)	YES	left frontotemporal craniotomy	78	65	63	85	85
20	right parietal glioma(HGG)	YES	right ftp craniotomy and excision	71	76	67	83	81
21	left temporoparietal glioma(HGG)	YES	left frontotemporal craniotomy	84	75	78	106	101
22	left parietal lobe(HGG)	YES	left frontotemporal craniotomy	55	65	67	94	91
23	right parietal glioma(HGG)	YES	right ftp craniotomy and excision	89	80	70	73	75
24	right parietal glioma(HGG)	YES	right ftp craniotomy and excision	76	56	56	91	82
25	left frontotemporoparietal glioma(HGG)	NO	left frontotemporal craniotomy	84	70	65	92	90
26	left temporal glioma(HGG)	YES	left frontotemporal craniotomy	70	65	64	98	80
27	right parietal glioma(HGG)	YES	right ftp craniotomy and excision	70	65	66	98	81
28	left fronto parietal glioma (HGG)	YES	left frontotemporal craniotomy	77	62	63	98	82
29	right frontotemporal glioma(LGG)	NO	right ftp craniotomy and excision	77	65	66	90	82
30	left fronto parietal glioma (HGG)	YES	left frontotemporal craniotomy	70	61	62	94	90

sl.no		SATURATION (SPO2)			RESPIRATORY RATE (BREATHS /MIN)			BISPECTRAL INDEX			OASS SCORE	
	AT T2	BASELINE	AT T1	AT T2	BASELINE	AT T1	AT T2	BASELINE	AT. T1	AT T2	BASELINE	AT T1
	after sedation	T0	after sedation	after sedation	T0	after sedation	after sedation	T0			T0	(after sedation)
1	90	100	98	98	15	12	11	93	80	70	5	4
2	78	100	100	100	16	13	12	98	70	75	5	3
3	88	100	100	98	14	11	12	98	80	70	5	4
4	100	100	99	98	12	10	11	98	79	77	5	4
5	89	100	100	98	14	11	14	95	76	67	5	4
6	95	100	98	99	16	12	13	99	77	80	5	4
7	83	100	98	100	15	13	12	97	75	67	5	4
8	81	100	100	98	14	10	13	95	72	78	5	4
9	91	100	100	99	16	14	11	93	74	79	5	4
10	80	100	100	98	15	13	12	84	70	77	5	4
11	100	100	100	98	14	15	12	99	65	70	5	4
12	85	100	100	99	15	13	12	95	67	70	5	4
13	91	100	97	100	16	13	12	98	79	70	5	4
14	88	100	98	98	14	11	12	97	80	77	5	4
15	80	100	98	100	14	12	12	98	80	79	5	4
16	91	100	98	100	16	13	13	96	76	78	5	4

sl.no		SATURATION (SPO2)			RESPIRATORY RATE (BREATHS /MIN)			BISPECTRAL INDEX			OASS SCORE	
17	90	100	98	100	15	13	11	95	76	75	5	4
18	80	100	99	98	14	11	13	99	66	67	5	4
19	85	100	98	99	14	14	11	100	70	68	5	4
20	81	100	99	98	12	14	11	98	65	77	5	4
21	91	100	98	99	13	10	12	99	67	76	5	4
22	85	100	98	99	13	11	11	92	78	70	5	4
23	76	100	98	98	14	14	12	98	77	70	5	4
24	80	100	99	100	15	14	12	96	75	76	5	4
25	98	100	100	100	14	12	10	94	77	79	5	4
26	85	100	98	100	14	13	12	99	73	77	5	4
27	83	100	99	99	14	12	11	99	70	75	5	4
28	80	100	100	100	14	12	12	99	70	77	5	4
29	80	100	100	99	16	12	11	99	70	65	5	4
30	91	100	99	98	14	12	11	100	70	60	5	4

sl.no		POST SEDATION		NIHSS SCORE							
	AT T2	t1	t2	CHANGE	N9		P13		N22		
	(after sedation)				AMPLITUDE	LATENCY	AMPLITYDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE
					(MICROVOLT)	(milliseconds)	(microvolts)	(milliseconds)(microvolts)(millisecs)			(MICROVOLT)
1	4	1	3	3	0.2	9.7	0.4	13.2	1.1	22.7	0.2
2	4	3	3	3	0.3	9.2	0.3	14.4	1.1	22.4	0.3
3	4	1	1	1	0.3	7.9	0.8	13.4	1.1	22.7	0.2
4	4	1	1	1	0.4	9.2	0.3	13.3	1	23	0.4
5	4	3	3	3	0.2	9.4	0.4	13.3	1	23	0.3
6	4	1	1	1	0.2	9.3	0.1	14	1.2	23.1	0.2
7	4	4	4	4	0.1	9.1	0.8	13.4	3	23.1	0.1
8	4	1	1	1	0.3	9.4	0.2	3.2	3.15	3.1	3.05
9	4	1	1	1	0.2	9.3	0.8	13.2	3	23.1	0.2
10	4	3	3	3	0.2	9.2	0.3	13.5	1.3	22.4	0.2
11	4	1	1	1	0.3	8.8	0.1	13.3	1.2	22.4	0.3
12	4	3	3	3	0.3	9.1	0.2	13.3	1.2	22.4	0.3
13	4	3	3	3	0.5	8.9	0.3	12.8	0.9	22.6	0.4
14	4	1	1	1	0.3	9.1	0.5	13	1.1	22.3	0.2
15	4	4	4	4	0.6	9.2	0.3	13.4	2	23	0.5
16	4	4	4	4	0.6	9.2	0.3	13.4	2	23	0.5

sl.no		POST SEDATION		NIHSS SCORE							
17	4	1	1	1	0.2	9.2	0.1	14	2	23.4	0.2
18	4	3	3	3	0.3	8	0.1	13.6	2	23.9	0.3
19	4	1	1	1	0.2	9.2	0.3	13.6	1.8	22.5	0.2
20	4	3	3	3	0.3	9.2	0.2	13.3	2	23.2	0.3
21	4	3	3	3	0.2	9.8	0.4	13.6	2	22.4	0.25
22	4	4	4	4	0.4	9.6	0.4	13.4	2	23.2	0.3
23	4	3	3	3	0.4	9.5	0.2	13.4	3	23.4	0.3
24	4	4	4	4	0.4	9.2	0.1	13.4	1.8	23.4	0.3
25	4	3	3	3	0.3	9.2	0.5	13.3	1	23.3	0.3
26	4	4	4	4	0.2	9.3	0.3	13.3	1.4	22.8	0.3
27	4	3	3	3	0.2	9.3	0.1	13.3	2	23	0.2
28	4	3	3	3	0.2	9.2	0.1	13.4	1	23	0.2
29	4	3	3	3	0.2	9.2	0.1	13.2	2	23	0.2
30	4	4	4	4	0.4	9	0.1	13.3	3	21.2	0.35

sl.no	tumour side t1					tumour side				
	N9	P13		N22		N9		P13		
	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE
	(milliseconds)	(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)	(MICROVOLT)
1	9.8	0.4	13.4	0.44	22.5	0.2	9.6	0.4	14	0.3
2	9.3	0.4	14.3	0.3	22.7	0.2	8.7	0.3	14.7	0.4
3	8	0.7	13.8	1.2	22.8	0.3	8.4	0.8	14	1.2
4	9.4	0.3	13.5	1.1	22.9	0.37	9.8	0.5	14	1
5	9.43	0.4	13.6	0.4	23.4	0.2	9.6	0.3	14	0.4
6	9.6	0.1	14.6	1.1	23.3	0.3	9.5	0.1	14.3	1.2
7	9.3	0.8	13.2	1	23.5	0.1	9.6	0.7	13.2	1.3
8	3	2.95	2.9	2.85	2.8	2.75	2.7	2.65	2.6	2.55
9	9.7	0.7	13.5	3	22.9	0.3	9.6	0.8	13.6	2.8
10	9.5	0.3	13	0.4	22.6	0.2	9.5	0.2	13	0.4
11	8.83	0.1	13.2	1.1	22.5	0.3	8.86	0.1	13.3	1
12	9.2	0.2	13.6	0.4	23.2	0.2	9.4	0.2	14	0.4
13	9.1	0.3	13.1	0.33	23	0.43	9.4	0.2	13	0.4
14	9.4	0.4	13.3	1	22.6	0.2	9.2	0.5	13.4	0.9
15	9.3	0.4	13.5	0.8	23.1	0.5	9.5	0.4	13.6	0.35
16	9.3	0.4	13.5	0.8	23.1	0.5	9.5	0.4	13.6	0.35

sl.no	tumour side t1					tumour side				
17	9	0.1	13.6	2.2	23.3	0.3	9.3	0.1	14.2	2.3
18	8.2	0.1	13.8	2	23.7	0.2	8.2	0.1	13.9	2
19	9.4	0.3	13.5	1.9	22.8	0.25	9.1	0.3	13.8	1.78
20	9.4	0.1	13.5	0.8	23.4	0.3	9.5	0.1	13.8	0.6
21	9.6	0.38	13.8	0.6	22.6	0.3	10	0.43	13.4	0.5
22	9.8	0.5	13.8	0.8	23	0.3	10	0.4	13.6	0.9
23	9.4	0.2	13.6	1.4	23.7	0.5	9	0.2	13.8	1.3
24	9.3	0.1	13.2	0.5	23.6	0.4	9.1	0.1	13.5	0.6
25	9.4	0.8	13.5	0.4	23.2	0.3	9.5	0.8	13.6	0.3
26	9.5	0.3	13.8	0.6	23	0.2	9.8	0.3	14	0.6
27	9.6	0.1	13.5	0.8	23.3	0.2	9.5	0.1	13.4	0.7
28	9.5	0.1	13.5	0.4	23.4	0.2	9.6	0.1	13.7	0.3
29	9.6	0.1	13.3	0.9	23.8	0.18	10	0.08	13.5	0.8
30	9.4	0.07	13.8	*1*	21.6	0.35	9.5	0.08	14	1.2

sl.no			NON TUM							
	N22		N9		P13		N22		N9	
	LATENCY		AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY
	(milliseconds)		(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)
1	22.6		0.1	8.3	0.4	14	1.1	22.3	0.1	8.5
2	22.3		0.2	8.8	0.3	13.7	1.1	23.8	0.2	9
3	23		0.3	9.1	0.4	11.8	1.23	22.8	0.27	9.2
4	23		0.3	9.2	0.3	12.6	1.3	22.5	0.3	9.5
5	23.5		0.2	9	0.4	13.2	1.4	22.5	0.3	9.3
6	23.4		0.1	9	0.2	13.1	1.2	22	0.1	9.4
7	25		0.3	9.6	0.2	13.4	3	22.8	0.3	9.8
8	2.5		0.2	8.9	0.4	13.3	1.3	22.8	0.2	9.3
9	23.3		0.2	9.5	0.2	13.5	3	23	0.3	9.6
10	22.8		0.2	9.9	0.3	13	1.5	22.2	0.2	9.8
11	23.1		0.2	9.1	0.1	13.3	1.1	22.3	0.2	9.2
12	23.3		0.2	8.9	0.2	13.3	1	23	0.2	9
13	22.7		0.4	9.2	0.1	13.4	2.3	22.8	0.45	9
14	24		0.2	9.1	0.5	13	2	22.8	0.24	9.3
15	23.2		0.8	9.3	0.2	13.2	1.2	22.4	0.7	9.5
16	23.2		0.2	9.2	0.3	13.2	1.1	23.3	0.2	9.4

sl.no			NON TUM							
17	23.5		0.2	8.8	0.2	14.1	3	23.4	0.2	9
18	23.9		0.5	9.5	0.3	13.2	1.4	23	0.4	9.7
19	23		0.2	9.2	0.3	13.6	1.8	22.5	0.2	9.4
20	23.5		0.4	9.4	0.2	13.5	1.6	23.3	0.3	9.6
21	22.5		0.1	9	0.3	13.2	2	23.2	0.1	9.2
22	22.7		0.2	9.2	0.4	13.3	2	23.4	0.25	9.3
23	23.8		0.3	9.4	0.1	13.4	1.5	23.8	0.3	9.6
24	23.6		0.1	9.3	0.4	13.2	1.8	23	0.1	9.5
25	23.4		0.4	9.2	0.3	13.4	2	23	0.4	9.4
26	23.6		0.3	9.4	0.2	13	1.4	22	0.3	9.8
27	23.5		0.3	9.1	0.1	13.2	1	22.3	0.3	9.4
28	23.5		0.3	9.2	0.2	13.4	1.8	23	0.3	9.4
29	23.9		0.3	9.2	0.2	13	2	21	0.2	9.6
30	22		0.1	9.4	0.1	13.4	3	23	0.1	9.8

sl.no	NON TUMOUR SSEP AT T1				NON TUMOUR SSEP AT T					
	P13		N22		N9		P13		N22	
	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY
	(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)	(MICROVOLT)	(milliseconds)
1	0.4	14	1.2	22.8	0.1	8.4	0.4	13.8	1.1	22.7
2	0.3	14	1.1	23.9	0.2	9.4	0.3	14.2	0.8	22.8
3	0.3	12	1.2	23	0.2	9.4	0.4	12.26	1.1	24
4	0.2	12.7	1.1	22.8	0.2	9.8	0.3	13	1.1	22.9
5	0.4	13.8	1.1	23	0.25	9.3	0.3	14	1.3	23.2
6	0.2	13.3	1	22.2	0.08	9.5	0.2	14	1.2	22.3
7	0.2	13.5	2.8	23.2	0.2	9.9	0.2	13.4	2.7	23.6
8	0.4	13.6	1.1	22.6	0.3	9	0.3	13.5	0.9	23.4
9	0.2	13.3	2.5	23.2	0.3	9.8	0.3	13.6	2.8	23.4
10	0.3	13.3	1.4	22.3	0.2	9.95	0.3	13.1	1.5	22.1
11	0.1	13.6	1.1	23	**0.2**	9.4	0.3	13.8	1	23.2
12	0.2	13	1.2	22.2	0.3	9.3	0.23	13.1	1.1	22
13	0.1	13.6	2	22.7	0.3	9.4	0.15	13.7	2.1	22.8
14	0.4	13.1	1.8	23	0.2	9.3	0.5	13.3	1.7	23.1
15	0.2	13.5	1.3	22.5	0.8	9.7	0.2	13.8	1.2	22.7
16	0.4	13.8	1.2	23.5	0.3	9.3	0.3	13.5	0.9	23.6

sl.no	NON TUMOUR SSEP AT T1				NON TUMOUR SSEP AT T					
17	0.2	13.8	2.8	23.2	0.35	8.9	0.23	14	2.9	23
18	0.3	13.4	1.2	23.4	0.4	9.6	0.35	13.7	1	23.2
19	0.3	13.5	1.9	22.8	0.25	9.1	0.3	13.8	1.78	23
20	0.2	13.9	1.5	23.4	0.4	9.7	0.2	13.7	1.4	23.8
21	0.2	13.3	2	23.4	0.1	9.4	0.3	13.6	1.8	23.3
22	0.4	13.6	2	23.6	0.3	9.5	0.4	13.5	2	23.9
23	0.1	13.6	1.2	23.2	0.4	9.8	0.1	13.8	1.4	23.6
24	0.5	13.7	1.9	23.2	0.13	9.6	0.4	13.4	1.7	23.4
25	0.3	13.5	1.8	23.3	0.3	9.5	0.3	13.9	1.7	23.2
26	0.2	13.2	1.3	22.8	0.2	10	0.2	13.6	1.2	22.6
27	0.1	13.5	0.9	22.6	0.3	9.6	0.15	13.6	0.8	22.8
28	0.2	13.5	1.6	23.3	0.4	9.6	0.2	13.6	1.5	23.5
29	0.17	13.4	1.6	21.6	0.2	9.8	0.16	13.6	1.4	21.8
30	0.1	13.5	2.7	23.2	0.1	9.8	0.07	13.6	2.5	23.4

sl.no					POST OP NIHSS(t3)	intraop fall in NIHSS specifications
	complications	interventions	INTRAOP COMPLICATIONS	POST OP DEFICITS		
		(needed/not needed)				
1	nil	not needed	nil	present	3	4,1,2
2	loc at BIS80	not needed	nil	present	3	6,4,5
3	nil	not needed	nil	absent	0	nil
4	nil	not needed	nil	absent	0	nil
5	nil	not needed	nil	present	3	4,3,1,2
6	nil	not needed	nil	present	3	4,3
7	nil	not needed	nil	present	0	4,3
8	nil	not needed	nil	absent	0	nil
9	nil	not needed	nil	prsent	2	4,3
10	nil	not needed	blood loss	absent	0	nil
11	nil	not needed	nil	absent	0	nil
12	nil	not needed	nil	present	0	nil
13	nil	not needed	nil	absent	0	nil
14	nil	not needed	blood loss	absent	0	nil
15	hypotension	inj mephentermine	venous air embolism	absent	0	nil
16	nil	not needed	nil	present	3	4,3

sl.no					POST OP NIHSS(t3)	intraop fall in NIHSS specifications
17	bradycardia	not needed	nil	absent	0	nil
18	nil	not needed	nil	present	0	4,3
19	nil	not needed	nil	present	3	4,3,5
20	nil	not neeeded	nil	present	3	4,3,5
21	nil	not neeeded	blood loss	absent	0	nil
22			nil	absent	0	nil
23	nil	not needed	nil	absent	0	nil
24	nil	not needed	nil	present	3	4,3
25	nil	not needed	nil	absent	0	nil
26	nil	not needed	blood loss	absent	0	nil
27	nil	not needed	blood loss	present	0	4,3
28	nil	not needed	blood loss	present	3	4,3
29	nil	not needed	nil	present	3	4,1,2
30	hypotension	not needed	nil	present	3	4,3

SL.NO	AGE	SEX	WEIGHT	Height	BMI	ASA(I/II)	SIZE OF TUMOR	volume of tumor	edema	midline shift	pre operative complaints	pre op steroids	pre op NIHSS
	(in yea	M/F	n kg	(in cms)			(in centimetres	(in cm3	yes/no)				P
1	26	M	47	155	19.5	I	1.8X1.7X2.3	7.03	YES	6.5 mm	SEIZURES, GAIT DISTURBANCEDEXAMETHASONE15	DEXAMETHASONE	0
2	52	F	90	166	32.72	I	4.7X2.5X4	47	YES	4 mm	GIDDINESS	DEXAMETHASONE	0
3	40	M	52	156	21.39	I	3X2.5X3	22.5	YES	3mm	HEADACHE	DEXAMETHASONE	0
4	45	M	60	165	22.05	II	2X3X3.2	19.2	NO	5mm	HEADACHE	NIL	0
5	31	F	83	165.6	30.51	I	2X4X2	16	NO	8mm	FOCAL SEIZURES	NIL	0
6	27	M	60	170	20.76	I	3x4x3	36	YES	4mm	HEADACHE	NIL	0
7	45	F	71	170	24.56	II	2X4X2	16	NO	3mm	HEADACHE	DEXAMETHASONE	0
8	30	M	50	155	20.83	II	1.8X2X2.2	7.92	YES	5mm	SEIZUES	DEXAMETHASONE	0
9	45	F	70	150	31.11	I	2X4X2	16	YES	5mm	HEADACHE	NIL	0
10	40	M	65	165	23.89	II	3X2X4	24	YES	6mm	HEADACHE	DEXAMETHASONE	0
11	27	F	56	156	23.04	I	3X3X5	45	NO	4 mm	HEADACHE ,SEIZURES	DEXAMTHASONE	0
12	32	M	58	158	23.29	II	3X2X5	30	NO	3mm	SEIZUERES	NIL	0
13	40	F	72	165	26.47	II	2X2X4	16	NO	5mm	SEIZUERES	NIL	0
14	33	M	60	155	25	II	3X3X5	45	YES	4 mm	HEADACHE ,SEIZURES	DEXAMTHASONE	0
15	29	F	70	160	27.3	I	2X3X2	12	NO	5mm	HEADACHE	DEXAMTHASONE	0
16	48	M	65	155	27.08	II	4X3X5	60	YES	3mm	MEMORY LOSS	NIL	0
17	40	F	60	156	24.69	II	4X3X5	60	YES	6mm	HEADACHE	NIL	0
18	32	F	67	160	26.17	I	3x4x3	36	NO	4 mm	HEADACHE ,SEIZURES	NIL	0
19	55	M	56	165	20.58	II	3X3X5	45	YES	8mm	HEADACHE	DEXAMTHASONE	0
20	45	F	60	155	25	I	3X2.2X3	19.8	YES	10mm	HEADACHE	DEXAMTHASONE	0
21	32	M	65	161	25.09	II	3X4X5	60	YES	5mm	HEADACHE	DEXAMTHASONE	0
22	54	F	66	158	26.5	II	2X4X3	24	YES	6mm	FOCAL SEIZURES	DEXAMTHASONE	0
23	44	M	64	162	24.42	I	5X5X3	75	NO	4mm	focal SEIZURES	NIL	0
24	40	M	58	158	23.29	I	4X5X3	60	NO	3mm	MEMORY LOSS	DEXAMTHASONE	0
25	21	M	75	160	29.29	II	3X4X5	60	NO	3mm	HEADACHE	DEXAMTHASONE	0

SL.NO	HERNIATION	TUMOUR DIAGNOSIS	PROCEDURE	HEART RATE (BE			MEAN ARTERIAL PRES			SATURATION (SPO2)			BISPECTRAL INDEX		
(ir	RESENT /ABSEN	(HGG/LGG)		BASELINE	AT T1	AT T2	ELIN	AT T1	AT T2	SELINE	AT T1	AT T2	ELINE	AT T1	AT T2
1	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	75	65	50	89	80	84	100	100	98	98	79	82
2	PRESENT	LEFT TEMPOROPARIETAL GLIOMA(LGG)	left ftp craniotomy and excision	80	60	55	90	85	84	100	97	98	98	80	82
3	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	75	66	60	88	80	84	100	100	98	100	80	77
4	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	80	65	66	90	85	82	100	100	99	98	83	71
5	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	88	80	77	90	86	84	100	100	99	98	79	70
6	ABSENT	LEFT TEMPOROPARIETAL GLIOMA(LGG)	left ftp craniotomy and excision	85	80	56	94	82	84	100	100	98	100	80	84
7	ABSENT	LEFT TEMPOROPARIETAL GLIOMA(HGG)	left ftp craniotomy and excision	90	80	50	90	80	86	100	99	99	100	80	89
8	ABSENT	LEFT TEMPOROPARIETAL GLIOMA(HGG)	left ftp craniotomy and excision	90	65	***55***	90	82	84	100	98	98	100	80	81
9	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	*92*	62	60	88	60	65	100	99	99	100	80	77
10	ABSENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	90	60	63	90	80	86	100	99	99	100	77	75
11	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(LGG)	right ftp craniotomy and excision	94	65	63	92	82	80	100	99	98	100	70	72
12	ABSENT	LEFT TEMPOROPARIETAL GLIOMA(HGG)	left ftp craniotomy and excision	90	60	63	90	70	72	100	99	98	100	83	80
13	ABSENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	94	61	60	92	80	88	100	98	98	97	82	80
14	PRESENT	LEFT TEMPOROPARIETAL GLIOMA(HGG)	left ftp craniotomy and excision	95	60	61	90	80	60	100	99	98	97	79	78
15	ABSENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	90	62	60	74	82	80	100	99	98	98	70	80
16	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	89	66	60	80	77	81	100	98	98	97	82	74
17	ABSENT	LEFT TEMPOROPARIETAL GLIOMA(LGG)	left ftp craniotomy and excision	80	60	61	80	77	88	100	98	97	98	77	76
18	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG0	right ftp craniotomy and excision	70	55	50	80	70	66	99	98	97	97	66	78
19	ABSENT	LEFT TEMPOROPARIETAL GLIOMA(HGG)	left ftp craniotomy and excision	70	65	50	89	77	65	99	98	98	95	77	81
20	ABSENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	77	66	51	90	70	65	100	98	98	90	66	82
21	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	76	56	50	78	65	60	100	98	98	96	75	77
22	PRESENT	RIGHT FRONTO PARIETAL GLIOMAA(LGG)	right ftp craniotomy and excision	86	65	68	90	65	60	99	98	97	99	81	70
23	ABSENT	LEFT TEMPOROPARIETAL GLIOMA(HGG)	left ftp craniotomy and excision	70	55	56	92	84	78	98	98	97	100	81	80
24	ABSENT	LEFT TEMPOROPARIETAL GLIOMA(HGG)	left ftp craniotomy and excision	78	65	60	85	80	89	99	98	98	99	81	82
25	ABSENT	RIGHT FRONTO PARIETAL GLIOMAA(HGG)	right ftp craniotomy and excision	89	65	66	94	81	80	100	98	98	100	81	80

SL.NO	OASS SCORE			POST SEDATION		NIHSS	TUMO						TUMOUI						TUM							
	(int	LIN	T T	T T	T T	T T	T:	CH	N9		P13		N22		N9		P13		N22		N9		P13		N22		
								AMPLITU	ATENC	MPLITU	LATENC	PLITU	LATENC	MPLITU	LATENC	MPLITU	LATENC	PLITU	LATENC	MPLITU	LATENC	MPLITU	LATENC	MPLITU	LATENCY		AMPLITUDE
								(microvol	lliseco	microvol	lliseco	microvo	lliseco	microvol	lliseco	microvol	lliseco	crovo	lliseco	microvol	lliseco	microvol	lliseco	microvol	lliseconds)		(microvolts)
1	5	4	4	1	1	1	0.2	9.2	0.7	13.4	1.8	21.3	0.2	9	0.7	13.6	1.8	21	0.3	9.5	0.5	13.9	2	21.1		0.2
2	5	4	4	1	1	1	0.3	9.3	0.1	13.3	2	19.2	0.28	9.3	0.1	13.5	2.2	19.7	0.33	9.5	0.15	13	1.8	19.4		2.8
3	5	4	4	1	1	1	0.4	9.1	0.2	13.2	3	20.2	0.35	9.3	0.2	13.8	2.8	20.6	0.3	9.4	0.16	14	2.75	21		0.3
4	5	4	4	1	1	1	0.3	9.4	1	11.4	0.6	21	0.25	9.2	1	11.6	0.6	21.2	0.28	9.5	1	11.1	0.5	21.6		0.4
5	5	4	4	1	1	1	0.3	9.4	0.1	13.2	2	22.2	0.3	9.6	0.1	13.1	1.8	22.4	0.24	9.66	0.08	13.5	1.7	22.5		0.6
6	5	4	4	1	2	2	0.3	9.1	0.2	11.2	3	21	0.25	9.3	0.2	11.4	2.8	22.5	0.28	9.3	0.2	11.5	21.5	22.6		0.6
7	5	4	4	1	1	1	0.5	9.2	0.1	11.1	2	20	0.4	9.4	0.07	11.7	1.6	21	0.35	9.35	0.08	11.5	1.5	21.3		0.4
8	5	4	4	1	1	1	0.8	9.4	0.3	11.3	1	20.1	0.65	9.7	0.25	11.6	0.8	21.4	0.7	9.8	0.24	11.8	0.8	21		0.3
9	5	4	4	1	1	1	0.25	9.8	0.34	10.7	2	20.8	0.24	10	0.32	13	1.9	21.1	0.2	10.1	0.3	13.2	1.7	21.3		0.3
10	5	4	4	1	1	1	0.6	9.1	0.4	13.2	1	20.5	0.56	9.3	0.35	13.4	0.7	20.8	0.53	9.4	0.36	13.6	0.8	21		0.5
11	5	4	4	1	1	1	0.4	9.2	0.2	13.1	1	20.2	0.34	9.6	0.18	13.3	0.8	20.8	0.36	9.8	0.19	13.4	0.8	20.9		0.3
12	5	4	4	1	1	1	0.3	9.1	0.1	12.9	3	21	0.27	9.5	0.12	13.3	2.6	21.8	0.25	9.6	0.08	13.7	2.8	21.7		0.4
13	5	4	4	1	1	1	0.4	9.2	0.2	13.1	2	21	0.34	9.4	0.18	13.4	1.7	21.5	0.36	9.8	0.19	13.6	1.8	21.7		0.3
14	5	4	4	1	1	1	0.2	9.4	0.1	13.1	3	21	0.18	9.6	0.1	13.4	2.7	21.5	0.17	9.8	0.1	13.6	2.8	13.7		0.3
15	5	4	4	1	1	1	0.5	9.4	0.2	13.2	4	21	0.45	9.7	0.18	13.5	3.4	21.5	0.4	10.1	0.17	14	3.2	21.7		0.3
16	5	4	4	1	1	1	0.4	9.1	0.3	13.2	3	21.2	0.34	9.5	0.25	13.4	2.4	21.6	0.32	9.7	0.2	13.5	2.2	21.8		0.3
17	5	4	4	1	1	1	0.2	9.1	0.1	13	3	22	0.17	9.2	0.09	13.4	2.4	23.1	0.18	9.4	0.08	13.6	2.6	23.5		0.3
18	5	5	4	1	1	1	0.3	9.2	0.2	13.2	1	21	0.24	9.5	0.18	13.6	0.8	21.8	0.22	9.7	0.15	14.1	0.7	22		0.4
19	5	5	4	1	1	1	0.3	9.3	0.4	13	2	22.4	0.25	9.6	0.3	13.4	1.5	23	0.24	10	0.32	13.6	1.7	23.3		0.2
20	5	4	4	1	1	1	0.4	9	0.2	13.1	2	21.4	0.35	9.4	0.15	13.4	1.5	22	0.3	9.6	0.14	13.7	1.4	23		0.4
21	5	4	4	1	1	1	0.2	9.2	0.3	13.1	2	21.2	0.15	9.5	0.2	13.5	1.6	22.4	0.14	9.8	0.24	13.7	1.4	23		0.3
22	5	4	4	1	1	1	0.2	9.1	0.3	13.2	1	21.2	0.16	9.6	0.2	13.6	0.7	21.7	0.13	9.8	0.23	13.8	0.6	22		0.3
23	5	5	4	1	1	1	0.2	11	0.4	13.2	3	21	0.16	11.4	0.32	14	2	21.4	0.15	11.6	0.3	14.2	2.2	22		0.5
24	5	4	4	1	1	1	0.3	9.2	0.3	13	2	21.3	0.2	9.6	0.2	13.4	1.7	22.1	0.22	9.8	0.23	13.8	1.3	22.6		0.4
25	5	4	4	1	1	3	0.3	9.1	0.3	13.2	1	22	0.25	9.4	0.23	13.5	0.6	22.6	0.2	9.6	0.2	13.7	0.6	23		0.2

SL.NO	NON TU					NON TUMOUR SIDE							
(in	N9	P13		N22		N9		P13		N22		N9	
	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY
	(milliseconds)	(microvolts)	(milliseconds)	(microvolts)	(milliseconds)	(microvolts)	(milliseconds)	(microvolts)	(milliseconds)	(microvolts)	(milliseconds)	(microvolts)	(milliseconds)
1	9.2	0.8	13.2	1.1	20.2	0.2	9	0.8	13.4	1.2	19.3	0.25	9.3
2	9	0.9	13.2	4	22.5	2.5	9.2	0.8	13.4	3.75	22.8	2.65	9.4
3	9.4	1	11.4	0.6	21	0.25	9.2	1	11.6	0.6	21.2	0.28	9.5
4	9.3	0.1	11.3	2	20.1	0.35	9.7	0.1	11.6	1.8	20.4	0.33	9.5
5	8.6	0.2	11.2	2	20.1	0.5	8.8	0.2	*11.6*	1.8	20.3	0.44	9
6	9.3	0.5	13.4	3	21	0.5	9.7	0.4	13.8	2.8	21.4	0.45	9.85
7	9.2	0.3	13.2	4	21.3	0.36	9.5	0.25	13.4	3.5	21.5	0.35	9.8
8	9.1	0.4	13.4	2	21	0.26	9.5	0.35	13.6	1.6	21.5	0.28	9.6
9	9.2	0.4	10.5	0.9	21	0.27	9.5	0.36	10.8	1	21	0.25	9.7
10	9.3	0.6	11	1	20	0.4	9.5	0.55	11.3	0.8	21.8	0.46	9.6
11	9.2	0.2	13	2	21	0.3	9.4	0.18	13.5	1.89	21.5	0.28	9.8
12	9.1	**0.1**	13	1	21	0.34	9.3	0.1	**13.3**	0.8	21.5	0.32	9.5
13	9.5	0.3	12	2	21.3	0.27	9.9	0.27	12.4	1.8	21.9	0.28	10.2
14	9.3	0.3	13.4	2	20.8	0.28	9.5	0.28	13.5	1.7	21.1	0.27	10.1
15	9.2	0.4	13.2	1	22	0.28	9.4	0.37	13.4	0.8	22.4	0.27	9.5
16	9.2	0.1	13	2	21	0.28	9.1	0.08	13.2	1.8	21.5	0.27	9.4
17	9.2	0.2	13.2	2	21.2	0.24	9.5	0.15	13.8	1.7	22	0.2	9.8
18	9.2	0.2	13	2	22	0.34	9.4	0.15	13.3	1.6	23	0.31	9.6
19	9.2	0.2	13	2	21.3	0.14	9.6	0.17	13.5	1.5	22	0.12	9.8
20	10	0.5	13.1	2	21	0.28	10.2	0.4	13.5	1.6	22	0.3	10.4
21	9.3	0.5	13.2	1	21	0.28	9.8	0.32	13.5	0.7	21.5	0.22	10.1
22	10	0.3	13	2	21.1	0.24	10.6	0.27	13.4	1.5	21.5	0.26	10.8
23	9.2	0.2	13.1	2	21	0.3	9.5	0.15	13.4	1.4	21.8	0.4	9.6
24	9.2	0.5	13	2	22	0.3	9.5	0.34	13.5	1.7	22.8	0.28	9.6
25	9.4	0.3	13	2	21.1	0.15	9.9	0.24	13.4	1.3	22.4	0.14	10

SL.NO	NON TUMOUR				COMPLICATIONS	INTERVENTIONS	INTRAOP	POST OP DEFICITS	POST OP	intraop fall in NIHSS
(in	P13		N22				COMPLICATIONS		NIHSS	(SPECIFICATIONS)
	AMPLITUDE	LATENCY	AMPLITUDE	LATENCY						
	(microvolts)	(milliseconds)	(microvolts)	(milliseconds)						
1	0.7	13.5	0.8	20.1	nil	nil	nil	absent	0	nil
2	0.8	13.5	3.5	23	bradycardia	inj atropine	nil	present	3	nil
3	1	11.1	0.5	21.6	nil	nil	nil	absent	0	nil
4	0.2	11.8	1.7	20.6	nil	nil	blood loss	absent	0	nil
5	0.2	11.3	1.7	20.5	nil	nil	nil	present	3	1,3
6	0.45	14	2.7	22	bradycardia	inj atropine	nil	present	3	3,4
7	0.26	13.5	3.8	21.8	nil	nil	blood loss	absent	0	nil
8	0.33	13.8	1.5	21.6	nil	nil	nil	absent	0	nil
9	0.35	10.9	0.7	21.4	nil	nil	nil	present	3	nil
10	0.55	11.5	0.8	21	nil	nil	blood loss	absent	0	nil
11	0.2	13.6	1.7	21.7	nil	nil	nil	present	2	nil
12	0.08	13.5	0.8	21.4	nil	nil	nil	absent	0	nil
13	0.26	12.6	1.7	22.1	nil	nil	nil	present	4	nil
14	0.27	13.8	1.6	21.4	nil	nil	nil	absent	0	nil
15	0.36	13.5	0.75	22.6	nil	nil	nil	absent	0	nil
16	0.07	13.5	1.75	21.8	nil	nil	nil	absent	0	nil
17	0.16	14	1.5	22.6	nil	nil	nil	absent	0	nil
18	0.18	13.6	1.5	23.3	nil	nil	nil	present	3	nil
19	0.15	13.8	1.4	22.4	nil	nil	nil	present	3	nil
20	0.42	13.8	1.7	22.3	nil	nil	nil	absent	0	nil
21	0.27	14.2	0.7	22	nil	nil	nil	present	4	nil
22	0.2	13.8	1.3	22.1	nil	nil	nil	absent	0	nil
23	0.14	13.6	1.2	22	nil	nil	nil	absent	0	nil
24	0.32	13.6	1.5	23.1	nil	nil	nil	present	3	nil
25	0.2	13.9	1.3	22.6	nil	nil	nil	absent	0	nil