Comparison of Effects of Propofol and Dexmedetomidine on Motor Evoked Potentials in Neurosurgery: A Prospective Randomised Single Blinded Interventional Study'

Dissertation submitted for the partial fulfilment for the requirement of the degree of

DM Neuroanaesthesia

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DECLARATION

I hereby declare that this thesis titled 'Comparison of Effects of Propofol and Dexmedetomidine on Motor Evoked Potentials in Neurosurgery: A Prospective Randomised Single Blinded Interventional Study' has been prepared by me under the capable supervision and guidance of Dr. Smita V., Associate Professor, Department of Anaesthesiology, Division of Neuroanaesthesia, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

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This is to certify that this thesis titled 'Comparison of Effects of Propofol and Dexmedetomidine on Motor Evoked Potentials in Neurosurgery: A Prospective Randomised Single Blinded Interventional Study', is a bonafide work of Dr. Soniya Biswas, DM Neuroanesthesia Resident, and has been done under my guidance and supervision at Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram. She has shown keen interest in preparing this project.

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ABBREVIATIONS

IONM	-Intraoperative neurophysiological monitoring
MEP (s)	-Motor evoked potential(s)
TcMEP	-Transcranial motor evoked potential(s)
CMAP	- Compound muscle action potential
MAC	- Minimum alveolar concentration
TIVA	-Total intravenous anaesthesia
SSEP(s)	-Somatosensory motor evoked potential(s)
AVM	-Arteriovenous malformation
TES	- Transcranial electrical stimulation
D waves	- Direct waves
I waves	-Indirect waves
M waves	- Myogenic waves
TMS	-Transcranial magnetic stimulation
DOA	- depth of Anaesthesia
BIS	-Bispectral index
PSI	-Patient State Index
EEG	-Electroencephalogram
EMG	-Electromyogram
SCTIMST	-Sree Chitra Tirunal Institute for Medical Sciences and Technology

Bpm	-Beats per minute
CNS	- Central Nervous System
HR	- Heart Rate
TOF	-Train of four
ASA	-American society of Anaesthesiologists
MAP	-Mean arterial pressure
GABA	- Gamma amino butyric acid
µg/kg	-microgram per kilogram
µg/kg/hr	-microgram per kilogram per hour
µg/kg/min	-microgram per kilogram per minute
mg/kg/hr	-milligram per kilogram per hour
mg/kg	-milligram per kilogram
ng/ml	-nanogram per millilitre
µg/ ml	-microgram per millilitre
mA	-milliampere
µV	-microvolt
V	-Volt
min	- Minutes
msec	- milliseconds
Hz	- Hertz

G	- Gauge
Kg	- Kilogram
Cm	- Centimetre
ICU	- Intensive Care Unit
RUL	- Right Upper Limb
LUL	- Left Upper Limb
RLL	- Right Lower Limb
LLL	- Left Lower Limb
%	- percentage
^{o}C	- Degree celsius
ANOVA	- Analysis of Variances

INTRODUCTION

Intraoperative neurophysiological monitoring (IONM) is often used in various intracranial and spine procedures to prevent damage to eloquent areas, cranial nerves or motor or sensory tracts. Motor evoked potential (MEP) monitoring is invariably an essential tool in the armamentarium of the operating surgeons to avoid injury to the motor tract in various intracranial and spine surgeries. (1)

Transcranial motor evoked potential (TcMEP) monitoring is stimulation of the motor cortex through the skull and eliciting compound muscle action potentials (CMAP) from the peripheral muscles to test the intactness of the motor pyramidal pathway. (1)

TcMEP is being used in surgeries for monitoring and mapping of the motor pathways. It is used in the mapping of the motor cortex in resection of tumours or arteriovenous malformations located near the motor cortex or in epilepsy surgeries. It is also used in the subcortical mapping of corticospinal tract. It is also used in brainstem surgeries and in Chiari malformation. It is also used in vascular surgeries like carotid endarterectomy, reconstructive surgeries of the neck, aneurysms of the aortic arch and of thoracoabdominal aorta or intracerebral aneurysms of middle or anterior cerebral arteries. It is very commonly used in spinal surgeries for extradural or intradural (extramedullary or intramedullary) tumour resection, embolization of arteriovenous malformations and in deformity corrective surgeries like scoliosis and spondylolisthesis. (2)

Intraoperatively, there are many factors other than surgical manipulation that can affect the quality of the CMAP like temperature, blood pressure, partial pressure of expired

carbon dioxide, oxygen, etc. These factors need to be optimized for correct interpretation of the MEPs. (2)

The anaesthetic agents can affect the quality of MEP intraoperatively as they inhibit synaptic transmission. Muscle relaxants antagonize the transmission of signals across the neuromuscular junction. Inhalational agents suppress the CMAP and should be used at a lower minimum alveolar concentration (MAC). Opioids seem to have very little effect on CMAP. Intravenous anaesthetics suppress MEP lesser than inhalational agents, so total intravenous anaesthesia (TIVA) or combination of intravenous with minimal inhalational anaesthetic supplementation is used when MEPs are monitored. (3)

TIVA with propofol and opioid is most commonly used for MEP monitoring. (4) As propofol gets rapidly metabolised, its sedative effects and effects on MEP can be adjusted quickly. But MEP can get depressed at high doses required to maintain surgical depth, hence, adjuvant agents that maintain anaesthetic depth without affecting the MEP are often required. (5)

Dexmedetomidine is a selective alpha-2 agonist. It causes sedation, analgesia, sympatholysis and minimal respiratory depression. (6) Its addition to the anaesthetic regimen can reduce hypnotic requirement, especially propofol. Dexmedetomidine has invariably been used as an adjuvant to various anaesthetic agents and has been found to have minimal affect on the MEP when combined with other agents. (7) It has found widespread acceptance in neuroanaesthesia because of its favourable recovery characteristics and absence of significant impact on cerebral blood flow and intracranial pressure.

REVIEW OF LITERATURE

MEPs are electrical signals measured from neural tissue or muscle when central motor pathways are activated. In TcMEP monitoring we stimulate the motor cortex with the help of scalp electrodes and elicit CMAP from the peripheral muscles. It gives an idea about the intactness of the motor pyramidal pathway. They complement other neurophysiologic monitoring techniques like somatosensory evoked potentials (SSEPs), as motor compromise can occur without sensory evoked potential warning, and vice versa. (2)

Uses of MEP

The discovery of transcranial electrical stimulation (TES) by Merton and Morton became a favoured method for corticospinal tract monitoring and has been used in the clinical setting since many years. It is used in many spinal and intracranial surgeries.

1) **Spinal cord surgeries** – There are various methods of intraoperative spinal cord monitoring.

Methods for intraoperative monitoring of spinal cord function

I) **Stagnara wake up test** – In this the patient is woken up intraoperatively after lightening the plane of anaesthesia and reversing the neuromuscular blockade and instructed to move the limbs to ensure the intactness of the motor tracts in the spinal cord. The test does not check the sensory tracts. It is not a continuous monitoring and intraoperative awakening with an endotracheal tube in situ can be a traumatic experience for the patient. (8)

II) **Ankle clonus test** – It is a test of historical interest. It was usually performed at the end of the surgery during emergence or at the time of the wake up test. The ankle is

sharply dorsiflexed to look for clonus. Its absence of which indicated spinal injury. It was a crude test. Factors like anaesthesia could affect its results. Its presence does not completely rule out spinal cord injury. (8)

III) **SSEP** – They are elicited by stimulating a peripheral mixed nerve and recording at a site cephalad to the area at risk.

The anterior two third of the spinal cord is supplied by the anterior spinal artery and posterior one third is supplied by the two posterior spinal arteries. The SSEPs can only detect damage to the dorsal aspects of the spinal cord. Patient can present with a postoperative motor deficit even after an intact intraoperative SSEP. Also SSEP signals require averaging of around 200 stimuli for eliciting a proper waveform which can delay the detection of a neural injury.

IV) **MEP** -A motor deficit is more devastating to the patient than a sensory deficit. But it is less reliable in patients with a preoperative neurological deficit. Also it cannot detect injury to the dorsal spinal cord.

V) **Combination of SSEP and MEP** – There is level 1 evidence that a combination of SSEP and MEP is a reliable adjunct to spinal cord monitoring to asses spinal cord integrity. (9)

The application of MEP monitoring in various types of spine surgeries is as follows

a) Spinal cord deformity surgeries

Combination of SSEP and MEP have almost replaced the traditional Stagnara wake up test especially in scoliosis and other spinal deformity correction surgeries. (10) In a

survey on SSEP monitoring alone in scoliosis surgery, Nuwer et al. had found that 0.063% of patients with intact SSEPs after surgery still had permanent neurological deficits and concluded that SSEPs are valuable but not adequate for monitoring the corticospinal tract of spinal cord. (11)

b) Spinal cord tumour resection

MEPs have become a standard of practice in spinal cord tumour resection surgeries which can be either extramedullary (intradural or extradural) or intramedullary. In many studies on spinal cord tumour excision surgeries where MEP monitoring was done, there were no reported cases of paraplegia or quadriplegia, (12, 13) and MEP monitoring significantly lowered the number of surgically induced injuries in the monitored group of patients. (14) Transient paraplegia has been reported postoperatively but the motor power recovered in a couple of hours or days if MEPs had been preserved intraoperatively. (12, 13)

c) Spinal AVM embolization

MEP monitoring can also be used during endovascular embolization of spinal cord arterio-venous malformation (AVM). A combination of SSEP and MEP monitoring has been used to identify vessels that supply functional grey and white matter distal to the tip of microcatheters so as to prevent their accidental embolization. This will prevent permanent neurological injury to the spinal cord postoperatively. (15)

2) Aneurysms of thoracoabdominal aorta

MEP monitoring has also been used during repair of aneurysms in thoracoabdominal aorta to detect spinal cord ischaemia. Jacobs et al had found that adjusting the

hemodynamic and surgical strategies according to changes in MEPs could restore spinal cord ischemia in most patients and prevent early and late paraplegia. (16)

3) Motor mapping

Monitoring muscle MEPs with short train stimuli can also be used for mapping motor cortex and subcortical motor pathways. It can be used in epilepsy surgeries and tumours involving motor cortex. In tumour excision surgeries located near motor area TcMEP is a feasible and safe monitor to predict and prevent postoperative weakness. (17)

4) Cerebral aneurysm surgery

In cerebral aneurysm surgery, MEPs can be used to recognize accidental clamping of perforating arteries supplying the capsular part of corticospinal tract. In this situation, SSEPs will remain unaffected but MEPs will disappear. If this condition is not recognized in time, there can be a postoperative pure motor hemiplegia.(18)

5) Intracranial AVM surgery

MEPs have also been used in intracranial brain AVM excision surgeries located near the motor cortex. Ichikawa et al had found that in AVM surgeries, MEP monitoring can help in the detection of blood flow insufficiency or direct injury of the corticospinal tract or the motor area. (19)

6) Brainstem and cervicomedullary junction surgeries

MEPs also show a high sensitivity in detecting motor deficits in surgeries involving space occupying lesions in the brainstem. (20) MEPs have also been used in combination with SSEP during foramen magnum decompression for Arnold Chiari malformation to detect intraoperative injury to the cervicomedullary junction and to predict postoperative neurological outcome. (21)

Motor pathways

The brain controls the voluntary and involuntary motor actions through somatic and autonomic motor system respectively. The somatic motor system consists of the upper motor neurons which carry majority of the signals from the Brodmann area 4 (motor cortex) and also signals from the premotor and supplementary motor areas and somatosensory areas via the corticospinal tract. The neurons of this tract arise from the pyramidal cells (Betz cells) present in the layer 5 of the cortex. The muscles of the various body parts are represented on the cortex in a particular fashion which is called as motor homunculus (Figure 1). Each cerebral hemisphere innervates the muscles of the opposite side. The homunculus is represented upside down along the precentral gyrus with facial muscles more inferiorly and laterally and leg muscles more medially and superiorly. The muscles which are involved in fine movements have more representation in the homunculus. Hence the hand muscles and muscles of facial expression have larger areas of representation as compared to trunk muscles. The nerve fibres after originating from the motor cortex pass through the posterior limb of the internal capsule. They then form the crus cerebri of the midbrain and pass through the ventral part of pons. 90% of the fibres decussate to the opposite side at the level of the medulla oblongata and form the lateral corticospinal tracts. Those fibres that do not cross form the anterior corticospinal tracts which descend down the spinal cord. These fibres decussate at the same level (in the anterior white commissure of the spinal cord) where they will synapse with the cell body of the lower motor neurons in the ventral horn of the spinal cord. Fibres from the lateral corticospinal tract also synapse at the ventral horns of the spinal cord. (22, 23) (Figure 2)

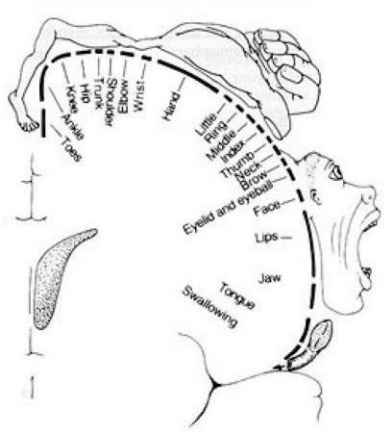

Figure 1 – **Motor homunculus**

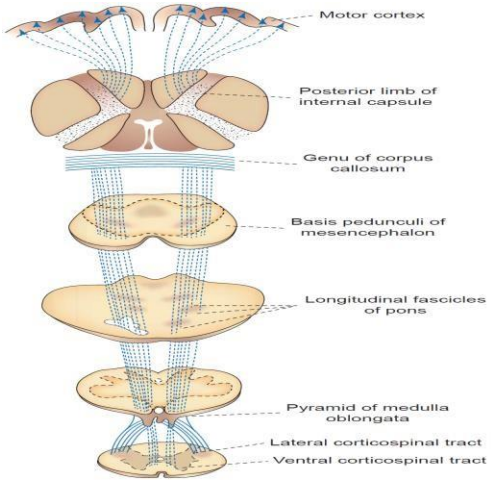

Figure 2 **Corticospinal tract**

The lower motor neurons start from the ventral horn cells (lamina VII and IX) of the grey matter of the spinal cord. The axons of the lower motor neurons exit the spinal cord and join their sensory counterparts of the same level and form the spinal nerves which finally innervate the skeletal muscles. They form a motor unit with the muscle fibres they innervate. A single motor neuron can innervate various muscle fibres. The connection between a nerve fibre and a muscle fibre is called neuromuscular junction where neurotransmitters are released which ultimately leads to muscle contraction. (22)

Both the neurons and muscle fibres are electrically excitable. The resting membrane potential of the muscle fibres is -60 mV. The potential is maintained by ion channels present in the cell membrane. Before a muscle contracts, there is depolarisation of the nerve fibres by generation of action potentials throughout the axon; which causes release of acetylcholine in the neuromuscular junction. Binding of acetylcholine to its receptors causes depolarization and generates action potential in the muscle sarcolemma. (22)

Compound muscle action potentials (CMAP) are a summation of action potentials of a group of muscle fibres.

Technique of MEP monitoring

MEP monitoring requires stimulation of the corticospinal tract either at the level of the cortex or spinal cord and recording of the evoked potentials either at the level of the spinal cord or the peripheral muscles.

Stimulation

Motor tract can be either stimulated directly at the level of the cortex or spinal cord or transcranially .

1) **Direct spinal stimulation** -Spinal cord stimulation is done intraoperatively and activates motor tracts but also excites sensory potentials and lower motor neurons via Ia afferent segmental synapses. (24) Hence, muscle responses cannot be attributed to only motor tracts. Spinal-elicited responses have been known to miss paraplegia after scoliosis surgery. (25) Spinally elicited muscle responses might be a valid way to monitor cauda equina motor axons when central motor tracts are not at risk. (26)

2) **Direct cortical stimulation** -The amount of current required to elicit MEP is considerably reduced (5–25 mA) and single pulse stimulus are usually sufficient. (27)
3) **Transcranial stimulation** – The stimulus is applied through intact skull which activates corticoefferent motor pathways without sensory stimulation. (28) Unlike the above mentioned techniques, either electrical or magnetic stimulation can be used.

a) **Transcranial electrical stimulation (TES) -**

Electrical stimulation of the motor cortex is done with

a) Surface electrodes (cup electrodes)
b) Needle electrodes
c) Cork screw electrodes

Surface electrodes are easy to place and non invasive but they are more prone to dislodgment and have higher impedance as compared to needle electrodes. Needle/corkscrew electrodes are most commonly used for TES (2) as they have lower impedance due to a larger contact area between electrode and tissue which prevents tissue injury from high stimulus currents by limiting current delivery to the tissue around the electrodes. They also have a lesser chance of displacement.

Site

The 10 – 20 montage system (American Electroencephalographic Society, 1994) (Figure 3) is used for the placement of the stimulating electrodes. (29)It is an international system used for applying scalp electrodes for the purpose of recording electroencephalogram (EEG). 10-20 refers to the distance between the electrodes which is described as the 10% or 20% of the distance between the nasion and inion and between the two auricles. Each

position is described by a letter which denotes the location of the electrode and a number. Odd numbers lie on the left side and even numbers on the right side.

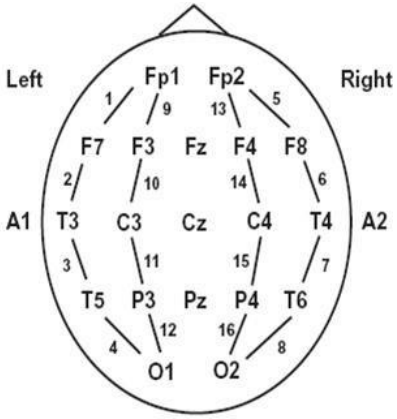

Figure 3 – **10-20 montage system**

While monitoring upper limb MEPs, stimulating electrodes should be placed at positions C3 and C4 and can be used to monitor right and left upper limbs by reversing the polarity.

For lower limb, electrodes can be placed at Cz and Fz. The Cz/Fz stimulating electrodes have the advantage of stimulating both the lower limbs simultaneously.

The C1/C2 stimulating electrode placement has the advantage of stimulating both upper and lower limbs with a single stimulus. (2)

Stimulus parameters

TES-MEP can be conducted with constant-voltage stimulators, which adjust the current to maintain the voltage, or constant-current stimulators, which adjust the voltage to maintain the current. When constant current stimulation is used, train frequency can be varied which is not possible with constant voltage stimulation. Thus to enhance MEP

during constant voltage stimulation intraoperatively a greater threshold current needs to be applied. This situation might arise when impedance increases with drop in body temperature intraoperatively. For constant current stimulation 40 – 200 mA current can be used. For constant voltage stimulation a maximum of 500 V can be used.

Single pulse TES is used for monitoring D waves (direct waves).When CMAP are being monitored under anaesthesia, multi-pulse TES (train of 3 to 9) is preferred as a single pulse is not enough to bring anterior horn cells to the firing threshold. (30)

If the interval between stimulus pulses in the train is very long, the post-synaptic potentials do not overlap and CMAP might not get elicited. If it is too short, stimuli are not effective in firing the corticospinal tract axons because of their refractory periods. (31) Thus, inter-pulse intervals between 2 and 4 ms (i.e., intra-train pulse repetition rates of 250 to 500 Hz) are optimal for generating CMAP. (2)

It is better to get baseline recordings with a set of stimulus parameters (stimulus intensity, number of pulses per train, and inter-pulse interval/pulse rate) under stable level of anaesthesia, and then adjust the parameters afterwards to obtain MEPs in each patient.

Transcranial electrical stimulation is easier to perform as the stimulating electrodes are smaller. Focal activation of a selective region of the motor cortex is also easier with electrical stimulation. The scalp discomfort that could be a major disadvantage of electrical stimulation in a conscious subject is not a problem during surgery under anaesthesia. (32)

b) **Transcranial magnetic stimulation (TMS)** -Magnetic coils are used for stimulation of the motor cortex. These are quite bulkier as compared to the needle electrodes used

for TES. There is a high degree of variability within the TMS elicited MEPs. (32) This variability can be due to technical factors like orientation, location, and stability of the TMS coil. (33) Magnetic stimulation is more diffuse so activation of a selective region is problematic. Also magnetic stimulation requires specialised equipment which cannot be used intraoperatively.

Recording of MEP

Type of responses

When the motor cortex is stimulated various types of responses can be elicited.

a) **D waves and I waves** -D waves or the direct waves are due to direct activation of the axons of the corticospinal tract and the I waves or the indirect waves which are due to indirect activation of the corticospinal tract from the interneurons. D-waves (elicited via single pulse stimulus) are recorded within the spinal cord using epidural/subdural electrodes. The electrodes should be kept rostral (for control) and caudal to the region at risk. As there are no synapses between the stimulating and recording site, multi-pulse stimulation is not required. D waves are resistant to the effects of anaesthesia and neuromuscular blockade. To improve signal-to-noise ratio averaging may be required. D-wave monitoring is not recommended below T10 because of the small number of corticospinal tract fibers below that level. (2) D wave monitoring is also not useful in cervical cord monitoring due to difficulty in placement of electrodes rostral to the involved level. Typical recordings use 10–20 ms time base, 5–20 sweep averaging, and 0.2–2 Hz to 1500–3000 Hz filtering. (26)

b) **M waves/CMAP** -When the transcranial stimulation causes the contraction of the peripheral muscles via the lower motor neurons originating from the anterior horn cells, CMAP or M waves are generated. (Figure 4) CMAP do not need signal averaging. CMAP requires synaptic transmission at the anterior horn cell for which train of stimulus pulses are required. CMAP are affected by anesthesia and neuromuscular blockade. (34) CMAP usually assess the spinal cord gray matter, which is more sensitive to ischemia than white matter, and also monitors nerve roots and peripheral nerves. (35) As CMAP need corticospinal tract conduction, anterior horn cell transmission and peripheral nerve conduction, they may be absent even if D-waves are present. (2) CMAP should be recorded from bilateral limb muscles. CMAP recording do not require averaging as they have good signal to noise ratio. Filter settings of 10–100 Hz to 1500–3000 Hz with 100 ms time base are appropriate. (26, 36)

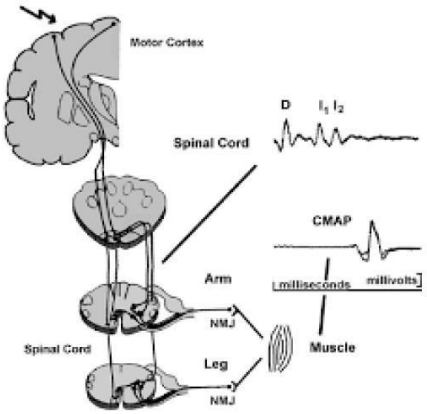

Figure 4 -**Response waveforms obtained after motor cortex stimulation**

Equipment

MEP monitoring systems are composed of a stimulating output, a recording input, an amplifier and a computing device. The stimulation unit must be isolated from the main portion of the stimulator circuitry to avoid a large current flow to the patient in the case of stimulator malfunction. An electrical grounding is necessary to prevent interfering signals from the power supply system. Equipment to avoid electromagnetic interference from cautery etc. should also be placed. (21)

Recording

Needle electrodes are generally preferred as they record larger signals than surface electrodes. The electrodes and their leadwires should be securely taped to the skin to prevent displacement. (2) Before the first measurement of MEP is taken up, a review of electrodes' impedances should be performed to ensure the correct position in the muscle and the correct signal transduction from the electrodes to the computing device. A ground electrode should be placed to improve signal quality and reduce stimulus artefact.

Site

In the upper limb, CMAP can be obtained from hand muscles (abductor pollicis brevis, abductor digiti minimi, or first dorsal interosseus muscles) because of their higher representation in the motor homunculus. For CMAP from abductor pollicis brevis, electrodes should be placed in the midpoint of palmar line drawn between first metacarpophalangeal joint and carpometacarpal joint. It can be made prominent by palmar abduction of the thumb. Proximal muscles can also be used. Upper limb MEPs are used during monitoring of the corticospinal tract in the cervical spinal cord, brainstem, or

the cerebrum. During the thoracic and lumbar spinal cord monitoring, upper limb MEPs can be used as a control to identify the effects of systemic factors like anaesthesia, that can affect the lower limb MEPs as well. (2)

Tibialis anterior and abductor hallucis are most commonly used for monitoring in the lower limbs. Proximal muscles can also be used, but they are less reliable. CMAP can also be recorded from anal sphincter during lumbar spinal cord surgeries especially cauda equina. (2)

For abductor hallucis, electrodes should be placed at half the distance between calcaneus and base of proximal phalanx of great toe. The muscle can be made prominent by spreading the toes.

MEP monitoring should be done bilaterally. A significant difference in the responses between the two sides can help detect unilateral pyramidal tract lesion.

Alarm criteria

a) **All or none phenomenon** – If there is inability to obtain CMAP in the lowest threshold muscle which was previously elicitable. (2)
b) **Threshold criteria** – increase in the threshold stimulus intensity required to get MEP (37)
c) **Amplitude criteria** – More than 50% drop (preferably upto 80%) in amplitude. The amplitude is measured between the most positive and negative points of the CMAP.
d) decrease in the CMAP duration and complexity (38)
e) **Latency criteria** – A 10% increase in latency.

Alarm criteria based on latency are usually not used during MEP monitoring. (15)

Complications of intraoperative MEP monitoring

During electrical stimulation of the corticospinal tract through the transcranial route, lighter anaesthesia plane and lack of muscle relaxants can cause complications like abnormal movements and muscle contraction, respiratory efforts, jaw jerks and tongue laceration and hemodynamic alterations like hypertension and tachycardia.

Seizures

Electrical brain stimulation can induce a sequence of abnormal neuronal discharges that can persist as after discharges sometimes progressing to a clinical seizure. Factors that can contribute to seizure occurrence are stimulus parameters, anaesthetic regimen and subject predisposition. (39)

Abnormal movement

There is a chance of accidental injury if patient movement happens during handling of a neural structure. Single pulse TES can avoid such abnormal movements. (40) With pulse train stimuli, the use of partial neuromuscular blockade can minimize the incidence of spontaneous movements. Though potentially dangerous in neurosurgeries multiple studies found the incidence of associated injuries were minimal. (39, 41)

Tongue bite

Tongue bite and rarely mandibular fracture have been reported during MEP monitoring due to jaw muscle contraction which can be prevented by using soft bite blocks. (39, 41) Since C3/C4 electrodes are nearer to the area presenting the facial muscles than C1/C2, stimulation at C3/C4 can produce stronger biting movements and cause tongue injury. (42)

Arrythmias

Arrhythmias due to hypothalamic stimulation or a seizure discharge are remote possibilities. (39) Cardiac pacemakers are a relative contraindication to TMS because there can be magnetic field disruption of the control circuitry.

Scalp injuries

There are no reports of scalp burns with TcMEP using 9-mm cup, adhesive or corkscrew or needle electrodes. The scalp discomfort of TcMEP is not relevant under anaesthesia. Headache due to scalp muscle contraction can occur after TMS, but there are no reports of headache resulting from TES -MEP monitoring. (39)

Contraindications

There are no absolute contraindications to MEP monitoring but there are a few relative contraindications like epilepsy, cortical lesions, convexity skull defects, raised intracranial pressure, cardiac disease, intracranial electrodes, vascular clips or shunts and cardiac pacemakers or other implanted biomedical devices. (39)

Effect of physiological parameters on MEP

There are multiple factors that can affect the MEP waveforms during intraoperative monitoring.

Temperature

The main effect of hypothermia on MEPs is prolongation of latency. An increase in MEP stimulation threshold is observed during anaesthesia as the body temperature decreases which can be due to decrease in motor cortical excitability or due to increase in impedance of recording electrodes.

Most of the reports suggest that the amplitude of the CMAP disappears below 28^0C. Systemic hyperthermia causes significant changes in the latency of CMAP. The latency changes of CMAP are usually significant at 2-2.5 C above or below baseline, suggesting a range within which evoked potential studies should be performed. (43, 44) Some suggest that the amplitude will not alter much if multi-pulse train is used. (45)

Regional spinal hyperthermia above 42°C slightly increase MEP latency and decrease the amplitude. When spinal cord temperature is more than 45°C, amplitude reduction becomes irreversible, suggesting permanent neural injury has occured. (46) Irrigation of spinal cord, brainstem, etc., with cold saline can cause alterations in evoked responses. (45)

Hypothermia can also change the plasma concentration of anaesthetics and neuromuscular blockade and influence the MEPs. Leslie et al. demonstrated that a drop in

temperature of 3°C would increase blood propofol concentration by 30% during constant infusion. (47)

Hypoxia

MEPs are not significantly affected by hypoxia until the partial pressure of oxygen in the tissue reaches levels that are associated with loss of ATP and cellular function. (48) Glucose deficiency further aggravates hypoxic inhibition of synaptic transmission. (49)

Blood flow and blood pressure

Mild to moderate reductions in blood pressure do not cause MEP changes. Reliable and reproducible spinal MEP potentials have been obtained in patients undergoing spinal surgery during deliberate hypotension to mean arterial pressures of 60 to 70 mmHg. (50) CMAP generated by transcranial stimuli reflect cellular function at the level of cortex, spinal cord and muscle. Ischemia at any of these sites can affect CMAP amplitudes. Even at normal systemic blood pressure, local factors can cause regional ischemia. At the level of the cortex, cerebral vasospasm and cerebral ischemia from retraction can affect CMAP. In spinal surgery, the effects of hypotension can get accentuated by spinal distraction, such that an acceptable limit of systemic hypotension cannot be determined without monitoring. (51) Peripheral nerve ischemia can occur from positioning and tourniquet placement.

Intracranial pressure

Raised intracranial pressure affects the cortical structures and causes a reduction in cortical responses. With increase in intracranial pressure there is a gradual increase in

latency of MEPs until it can no longer be produced. Loss of brainstem responses results with onset of uncal herniation. (34)

Carbon dioxide

Changes in the partial pressure of carbon dioxide within the normal physiological range do not affect the CMAP.

Hypercapnia has depressive effects on cortical and anterior horn cell excitability and peripheral neuromuscular transmission. (52) Animal studies suggest that hypercapnia (upto 100 mm Hg) increases latency and decreases amplitude of MEP. (53)

Hypocapnia may facilitate cellular transmission at spinal level. (53) Hyperventilation upto 13 mm Hg has not shown any change in CMAP in both human and animal models. (54)

Effects of anaesthetic agents on MEP

The anaesthetic agents modulate the activity of various ion channels and neurotransmitters like gamma amino butyric acid (GABA), N-methyl D aspartate, etc. and thus reduce the synaptic transmission through the cortex, spinal cord and neuromuscular junction. As neurophysiological monitoring assesses the integrity of the central and peripheral nervous system and their synaptic transmission, the recordings can get depressed by the anaesthetic agents. The cortex, anterior horn of spinal cord and neuromuscular junction are most susceptible to the anaesthetic effects on MEPs. The degree and type of affect will depend upon the anaesthetic agent used and the number of

synaptic connections involved. TcMEPs are very sensitive to anaesthetic agents especially inhalational agents.

Inhalational agents

Volatile anaesthetics such as halogenated agents have an effect on both cortical pyramidal neurons and interneurons by increasing GABA mediated inhibition. (55) Burke et al. (56) suggested that halogenated agents significantly decrease the transmission of impulses at the nodes of Ranvier and thus decrease the excitability of the corticospinal axons. Also halogenated agents have a suppressive effect at the spinal level by suppressing the synaptic transmission at the alpha motor neurons.

Volatile anaesthetics, including nitrous oxide and halogenated agents cause a dose-dependent depression of both CMAP and I waves. They increase latencies, increase mapping threshold of stimulation and decrease amplitude. Simultaneous use of nitrous oxide and halogenated agents has a synergistic depressive effect on MEPs. MEP recording is possible only at low concentrations, for example at 0.2-0.5% of halogenated agent.

D waves are least affected by anaesthetics but inhalational anaesthetics can increase the latency and decrease the amplitude of D waves. (56)

Volatile suppression can be partially overcome by using higher-intensity and multi-pulse stimulation. (57 -60)

Woodforth et al., (60) recorded CMAP in response to single pulse stimulation in patients anaesthetised with fentanyl and 70% nitrous oxide and found that MEP amplitudes were very low.

An animal study comparing the effects of halothane, isoflurane and enflurane on MEP by Zetner et al found that there is a dose-dependent suppression of the CMAP responses, which was similar with all anaesthetics. Beyond 0.5 MAC of any of the agents, CMAP were absent. In contrast, D waves were only slightly affected by the anaesthetics. (61)

Pelosi et al found that, isoflurane at concentrations of 0.75 and 1 MAC, produce adequate CMAP responses in only 61% and 8% of patients, after multi-pulse transcranial electrical stimulation. When compared to propofol based anaesthetic regimen, the CMAP amplitudes were lower and reproducibility was lower. (62)

Chong et al had found that sevoflurane used in increasing MAC from 0.3 to 0.5 to 0.7 depressed MEP amplitude from baseline to 66.2%, 41.3%, and 25.3% respectively. Desflurane at 0.3 MAC produces reliable MEP but at 0.5 and 0.7 MAC depressed MEP amplitude to 58.4% and 59.9% of baseline. Sevoflurane depressed MEPs more as compared to desflurane. (63)

Hernandez et al had compared the effects of propofol and sevoflurane on TcMEP and SSEP in brainstem surgeries and had found that 0.5 MAC sevoflurane or propofol at an effect-site concentration of 2.5 µg/mL (50-75 µg/kg/min) for maintenance of anaesthesia with a background infusion of remifentanil (0.25 to 0.35 µg/kg/min) and cisatracurium (0.03 to 0.04 mg/kg/h) had similar effects on TcMEP ie. decrease in amplitude and increase in latency. Even though the amplitude was higher and latency was shorter in

propofol group (statistically significant) as compared to sevoflurane group but it was not clinically significant. (64)

Intravenous anaesthetics

Propofol

Propofol causes depression of cortical activity by selectively suppressing L-type calcium channels in cortical neurons, as well as opening GABA(A) gated chloride channels. (65) Propofol also suppresses activation of alpha motor neuron at the level of the spinal gray matter.

The rapid metabolism and titratability of propofol have made it a popular anaesthetic agent of choice for use during MEP monitoring in cases which require early postoperative emergence for neurologic examination. (66) Multi-pulse stimulation techniques can improve response amplitudes and monitoring success under propofol anesthesia. (67) When serum propofol levels are maintained at or below 1 µg/mL (20–25 µg/kg/min) and supplemented by opioid/50% N2O, transcranial electric stimulation applied in 2 to 6 pulses produced CMAP responses in 100% of patients. (68) Serum propofol concentrations between 1 to 2 µg/mL (25–50 µg/kg/min) caused a 30% to 60% reduction in CMAP amplitude despite multi-stimulus techniques, even though response acquisition and reproducibility were well maintained. (68) Above 3 µg/mL (75–100 µg/kg/min), greater variability in response depression has been reported, ranging from 33% to 83% in CMAP amplitude. (69) Response acquisition was adequate in only 60% to 88% of patients above this serum concentration. (69) Scheufler and Zentner used transcranial magnetic stimulation to demonstrate the effects of propofol as a single agent. At plasma propofol levels of 3 mcg/mL (75–100 µg/kg/min), increasing stimuli rates

from 2 to 4 pulses more than doubled CMAP amplitudes. At higher serum propofol levels (≥5 μg/mL [>100 μg/kg/min]), a greater amplitude depression was seen despite increasing number of impulses, although CMAP responses were recordable. (70)

Benzodiazepines

Benzodiazepines enhance GABA-ergic cortical inhibition by interacting with GABA receptor. Studies suggest that the excitability of the pyramidal cells is reduced during sedation with short-acting benzodiazepines (like midazolam) due to an enhancement of the inhibitory action GABAergic cortical interneurons. (71) The use of benzodiazepines results in a significant reduction of the amplitudes of MEPs and increase in the cortical mapping threshold. (72)

Barbiturates

Their mechanism of action is similar to benzodiazepines. Induction bolus can abolish MEPs for 45-60 min.Thiopentone has a significantly lower incidence of MEP preservation (20%) as compared to methohexital (50%). (73)

Etomidate

Animal studies have shown that at low dose (0.1 mg/kg) etomidate has an excitatory cortical effect but at high doses (≥ 0.9 mg/kg) it has a depressive effect on TcMEP. Etomidate usually affects the amplitude of MEPs. (74)

The influence of four intravenous anesthetic agents on MEPs elicited by TMS was studied by Taniguchi et al. The patients were anaesthetized by a continuous intravenous infusion of propofol, etomidate, methohexital, or thiopental. To ensure comparable effects on level of anaesthesia by each of the agents, an infusion scheme for each of the

drug was computed. A dose-related reduction of the MEP amplitudes was seen in all drug groups, while the latencies remained constant. MEPs were obtainable at the end of induction in 14% of the propofol group, 57% of the etomidate group, 53% of the methohexital group and 20% of the thiopental group. Propofol and thiopental showed significantly stronger suppression of MEP as compared to etomidate (both $P < 0.01$) and to methohexital ($P = 0.01$ and 0.05, respectively). Etomidate was the least detrimental agent for intraoperative monitoring of magnetic MEP. (75)

Ketamine

The effect of ketamine on MEP is inconsistent. Glassman et al found that ketamine enhances MEP (76); while Yang et al observed a non significant decrease in the amplitude of the MEPs with an increase in latencies. (77) The higher the doses, more likely is the suppression of MEPs with ketamine.

Opioids

Opioids are used mainly for their analgesic effects and have minimal effects on MEPs. A bolus dose up to 3 mcg/kg fentanyl does not significantly alter CMAP amplitude. (78) By decreasing the background spontaneous muscle contractions and associated motor unit potentials, fentanyl can improve the myogenic responses. The effects of the opioids fentanyl, alfentanil, and sufentanil on MEP were studied by Thees et al in rabbits. They concluded that all the three opioids caused a dose dependent suppression of MEP amplitudes with a greater suppression by fentanyl as compared to sufentanil and alfentanil. At plasma concentrations maintaining an adequate surgical level of analgesia, monitoring of MEP with opioid infusion is feasible. (79)

Muscle relaxants

In the presence of a deep blockade, CMAP cannot be elicited. Use of neuromuscular blockade is completely avoided for monitoring CMAP ideally. But partial neuromuscular blockade can be used to avoid unwanted movements during the surgery and to allow easier retraction of the muscles by the surgeon. Neuromuscular blockade can be evaluated using TOF count or ratio or by comparing the height of twitch response to single pulse stimulation before and after giving the muscle relaxant. Because of varying sensitivity of different muscles to muscle relaxants, the blockade should be monitored in the same muscle groups used for electrophysiological monitoring. (34)

In a study by Kim et al on neurosurgical patients who required intraoperative MEP monitoring, they found that avoiding neuromuscular blockade led to better MEP monitoring parameters without an increased incidence of hypotension or spontaneous movement and respiration as compared to partial blockade. Partial blockade minimally reduced the MEP amplitudes of upper extremities but the amplitudes of lower extremities were decreased in all patients with partial blockade, possibly due to the different sensitivities of muscle groups to neuromuscular drugs. (80)

Techniques to overcome anaesthetic depression

Multi pulse stimulation technique

As mentioned before multi pulse stimulation can improve CMAP response under anaesthesia.

Titration of anaesthetic drugs

As the concentration of anaesthetic agents like propofol and halogenated volatile anaesthetic agents is increased, there is a depression of MEP waveforms. To get adequate and reproducible waveforms the doses of these anaesthetic agents need to be reduced. But this might lead to a decrease in the anaesthetic depth which will interfere with the surgery as well as cause discomfort to the patient This can be achieved either by using a combination of low dose of various anaesthetic agents or by using adjuvants which can decrease the requirement of the anaesthetic agents while providing an equivalent anaesthetic effect, but with little effect on MEP.

Combination of drugs

Propofol (75–125 µg/kg/min) along with low dose desflurane (0.3 MAC) has been shown to produce minimal effects on MEP as compared to baseline. (63) A similar combination of propofol with low dose sevoflurane (0.3 and 0.5 MAC) depressed CMAP amplitude to 66.2% and 41.3% of the baseline respectively. (63)

Adjuvants

Various agents have been used as adjuvants to decrease the requirement of the anaesthetic agents especially propofol which is most commonly used for MEP monitoring.

Ketamine is a valuable adjunct to TIVA anaesthesia for surgical cases that need MEP monitoring. Extra caution needs to be taken for its side effects such as hallucinatory potential, increase in the intracranial pressure with intracranial pathology and triggered

epileptic activity in cases of functional cortical mapping, where it can lower the threshold for stimulation. (77)

Dexmedetomidine

Dexmedetomidine is an alpha-2 adrenergic agonist. It has sedative, anxiolytic, sympatholytic and minimal respiratory depressant effect. (6) Dexmedetomidine has been used invariably in intensive care units and perioperatively. It has been used as a premedication (0.33 -0.67 µg/kg 15 minutes before procedure), as an anaesthetic and opioid sparing agent intraoperatively (loading dose followed by maintenance), for postoperative analgesia, for sedation in intensive care units (loading dose not required) and during procedures like awake fibreoptic intubation, radiological investigations and as an adjunct to regional anaesthesia. In neuroanaesthesia it has been used during surgeries like awake craniotomy, deep brain stimulation, etc. (81)

Effect on hemodynamics

Dexmedetomidine is administered with a loading dose of 0.5-1 µg/kg in first ten minutes and then a continuous infusion of 0.2-0.7 µg/kg/hr. After the initial loading dose there can be either hypertension or hypotension and bradycardia. The hypertensive response is mainly due to the vasoconstrictive effect of alpha-2 adrenoceptor stimulation and is most commonly seen if the loading dose is given over ten minutes. Giving the loading dose over twenty minutes can reduce the incidence of hypertension. Hypotension and bradycardia are mostly associated with a large loading dose. Avoiding the loading dose or reducing it (eg. 0.5 µg/kg) makes hypotension less pronounced. During maintenance, usually a lower mean arterial pressure and heart rate from the baseline is seen. (81)

Chakrabarti et al found that dexmedetomidine infusion as an adjuvant to propofol reduced mean arterial pressure and heart rate in cerebellopontine angle surgeries (82) In patients undergoing MEP monitoring during neurosurgery dexmedetomidine was found to decrease the heart rate as compared to propofol. The mean arterial pressure was found to be lower with use of dexmedetomidine. (83, 84) Li et al (85) found that when dexmedetomidine is used as an adjuvant to propofol, mean arterial pressure was higher as compared to propofol alone.

Effect on CNS

Dexmedetomidine has sedative, analgesic, anaesthetic sparing and sympatholytic effects.

Its analgesic action occurs at spinal and supraspinal levels. Dexmedetomidine causes alpha-2 receptor mediated activation of inwardly rectifying potassium gated channels which leads to membrane hyperpolarisation and inhibits firing of the neurons in the substantia gelatinosa of spinal cord. This will in turn inhibit the release of nociceptive neurotransmitters like substance P. Dexmedetomidine also decreases the influx of calcium ions into the cells and inhibits the release of nociceptive neurotransmitters.

Noradrenergic neurons in the locus coeruleus have a high density of alpha-2 receptors. Activation of these receptors causes hyperpolarisation of these neurons and thus inhibiting them from firing. Inhibition of this firing leads to release of GABA from the preoptic and tuberomammillary nuclei which in turn inhibits the release of histamine in the cortex and subcortical pathways. This inhibition is the main cause of the drug's sedative action. Analgesic effects are also supplemented by the modulation of the neurotransmitters in the locus coeruleus.(81) Wei et al found that a single dose of

dexmedetomidine (1 µg/kg) facilitated intubation following induction with propofol and remifentanil without using muscle relaxants pointing towards a possible muscle relaxant effect of dexmedetomidine. (86)

Dexmedetomidine produces sedative action by hyperpolarizing the noradrenergic neurons in locus coeruleus. Since it has no action on cortical EEG, the level of sedation produced by dexmedetomidine cannot be ideally evaluated by standard depth of anaesthesia monitors which depend on processed EEG.

Depth of anaesthesia monitors

Depth of anaesthesia monitoring is essential during IONM for titration of anaesthetic drugs. It can be used as a guide to titrate the depth of anaesthesia without increasing the risk of awareness for optimal MEP monitoring. Processed EEG is most commonly used for the same. All depth of anaesthesia monitors use processed EEG to obtain a dimensionless digital number which is easier to interpret. Raw EEG information is obtained mostly from the frontal region. The EEG signal is then filtered and amplified, digitised and sent to the device for mathematical processing. The raw EEG is usually divided into time segments/epochs and processed as segments. Of the different depth of anaesthesia monitors Bispectral index (BIS) is the most commonly used modality.

BIS

It has a frontal montage sensor and picks up the raw EEG signals from the frontal region and converts it into a number between 0 (isoelectric EEG) to 100 (fully awake). Its calculation algorithm involves power spectrum, bispectrum, relative activity in the beta frequency range, synchronised fast slow activity and burst suppression activity. Apart

from the BIS value it also displays the signal quality index, burst suppression ratio, EEG and EMG (electromyogram). A value between 40 and 60 indicates adequate depth of anaesthesia. (87)

Various studies have used BIS monitoring when dexmedetomidine has been used as an adjuvant to propofol/remifentanil/desflurane/fentanyl and have not reported any incidence of intraoperative awareness. (83 – 85, 88 - 90)

PSI (Patient State Index)

PSI was approved by FDA in 2000 and uses a four channel frontal EEG montage. The monitor displays the PSI value (0 -100), density spectral array from both the sides, unprocessed EEG and EMG, artefact index and burst suppression ratio. Adequate depth of anaesthesia corresponds to a value between 25 and 50. Many studies have found a good correlation between PSI and BIS values in propofol/etomidate/ thiopentone/sevoflurane based anaesthesia. (91-94)

A few studies also found a correlation between PSI values and depth of anaesthesia and sedation in dexmedetomidine based anaesthesia. (95, 96) Sayed et al had found that in living donors for liver transplantation, PSI guided dexmedetomidine infusion helped to reduce desflurane and fentanyl consumption with no adverse effects on hemodynamics. (96)

Effect on MEP

It has been used as an adjuvant to propofol during MEP monitoring to reduce propofol dose requirement . Most of the studies suggest that dexmedetomidine do not reduce the

amplitude or latency of MEP significantly when used as an adjuvant. (83, 85, 88 - 90). Most of these studies have used a loading dose of 0.5 to 1 µg/kg followed by a maintenance infusion of 0.5 µg/kg/hr.

Li et al used dexmedetomidine as an adjuvant to propofol and remifentanil and found that it did not have any significant effects on amplitude and latency of MEPs in spinal tumour surgeries as compared to propofol and remifentanil combination. The average dose of dexmedetomidine used in their study was 0.5 µg/kg loading followed by 0.5 µg /kg/hr. (85)

Anschel et al studied 18 subjects undergoing scoliosis surgery with propofol and dexmedetomidine based anaesthesia. They concluded that dexmedetomidine, when used as part of a TIVA regimen, offered the characteristics of both an anaesthetic and analgesic and did not significantly obscure the recording of either sensory or motor evoked potentials and provided the patients with a relatively easy awakening and recovery postoperatively. (88)

Rozet et al in their study of 40 patients who underwent spine surgeries with propofol, remifentanil and dexmedetomidine also found that in clinically relevant doses, dexmedetomidine as an adjunct to TIVA does not seem to alter MEPs and therefore can be safely used during surgeries requiring monitoring of MEPs. (90)

Bala et al used dexmedetomidine (upto 0.6 ng/ml plasma concentration) as an adjuvant to desflurane and remifentanil and found that it did not affect the amplitude or the threshold current required to obtain MEP significantly. (84)

A few studies found that dexmedetomidine can cause suppression of MEP especially after the loading dose. (99, 100) These studies have used a loading dose of 1 µg/kg calculated on the basis of total body weight. Mahmoud et al studied 40 patients who had posterior spinal fusion surgery during propofol and remifentanil anaesthesia with dexmedetomidine as an adjuvant. The authors concluded that dexmedetomidine as an anaesthetic adjunct to propofol-based TIVA at clinically relevant target plasma concentrations (0.6–0.8 ng/ml) can significantly decrease the amplitude of TcMEP. (100)

In our study, we used dexmedetomidine as an adjuvant to low dose sevoflurane and compared its effect on amplitude and latency of motor evoked potentials with that of propofol.

Rationale of the study

Intraoperative MEP monitoring is often compromised by the use of anaesthetic agents that can depress the MEP waves. Both propofol and sevoflurane are seen to have a dose dependent depressive effect on TcMEP responses. Though propofol is the preferred agent in the IONM, it too can produce suppression of MEP in doses required to maintain adequate depth of anaesthesia. In his study on TcMEP and SSEP in brain stem surgeries, Hernandez et al (64) had found that both 0.5 MAC sevoflurane and propofol infusion at effect site concentration of 2.5 µg/ml had similar effects on MEPs. The low doses required to maintain adequate MEP monitoring cannot produce an adequate depth of anaesthesia. Thus an adjuvant to these agents is required which will facilitate MEP and at the same time maintain an adequate depth of anaesthesia. And also an adjuvant to either low dose propofol or sevoflurane should have similar effects on MEP.

Dexmedetomidine is an alpha 2 agonist which has a sedative, anxiolytic, sympatholytic and anaesthetic sparing effect. Few studies have also suggested a muscle relaxant effect of dexmedetomidine. (86) There are many studies which have evaluated the effects on MEP of dexmedetomidine as an adjuvant to low dose propofol but similar studies with sevoflurane are lacking.

In our study, we have evaluated the effects on MEP of dexmedetomidine as an adjuvant to low dose sevoflurane and compared it to the effects that a combination of anaesthetic regimens - propofol and low dose sevoflurane will have on MEP monitoring in neurosurgery. We have also compared the hemodynamic stability and recovery parameters and complications between the two anaesthetic regimens. This study will help in formulating an anaesthetic plan which can be used in neurosurgeries where motor evoked potentials monitoring can be performed without causing hemodynamic instability or intraoperative awareness and at the same time facilitating MEP acquisition and surgical procedure so that intraoperative and postoperative complications can be avoided.

HYPOTHESIS

Research Hypothesis – Dexmedetomidine in combination with low dose sevoflurane produces less suppression of amplitude and latency of motor evoked potentials when compared to a combination of propofol and low dose sevoflurane in patients undergoing neurosurgery

Null Hypothesis – There is no difference between the effects of dexmedetomidine and propofol in combination with low dose sevoflurane on amplitude and latency of motor evoked potentials in patients undergoing neurosurgery

AIMS AND OBJECTIVES

Aim – To compare the effects of propofol and dexmedetomidine on the amplitude and latency of MEPs in patients undergoing neurosurgery

Objectives – **Primary**

1) Compare the effects of propofol and dexmedetomidine on amplitude and latency of motor evoked potentials in patients posted for neurosurgery who require MEP monitoring intraoperatively

Secondary

2) To compare the hemodynamic parameters of the two anaesthetic regimens containing propofol and dexmedetomidine during the surgery

3) To compare the recovery profile at the end of the surgery between the two anaesthetic regimens containing propofol and dexmedetomidine

3) To compare the complications of the two anaesthetic regimens containing propofol and dexmedetomidine during the surgery

MATERIAL AND METHODS

The study was a prospective randomised single blinded interventional study conducted in the neurosurgery operation theatre of Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Thiruvananthpuram. Adult patients of age group 18-60 years presenting for any spinal or intracranial surgery requiring MEP monitoring as part of their operating procedure were considered for recruitment in a consecutive manner between 1st January 2018 and 31st December 2018.

Inclusion criteria:

- Patients presenting for any spinal or intracranial surgery for a lesion involving the motor cortex or pyramidal tract requiring intraoperative MEP monitoring`
- Age 18-60 years

Exclusion criteria

- Patient refusal
- Age less than 18 years and more than 60 years
- Autonomic instability
- Long standing Diabetes mellitus (>10 years)
- Pregnant & nursing mothers
- Motor power grade <3
- Neuromuscular disease
- Cardiopulmonary disease
- Skull defects at the region where electrodes need to be placed
- Intracranial apparatus (electrodes, vascular clips and shunts), cardiac pacemakers or other implanted pumps

- Renal and hepatic disease
- History of chronic alcohol use
- Allergy to any of the anaesthetic agents used in the study
- Preoperative heart rate <50 bpm (beats per minute), presence of heart block
- Patients on antihypertensive medication with alpha methyl dopa, clonidine
- Patient on beta blockers

After getting approval from the technical advisory committee and institutional ethics committee of SCTIMST and Central Trial Registry of India (CTRI/2018/07/014709), the study recruited cases from January 2018.

Informed consent was taken from patients satisfying the inclusion criteria and consenting patients were included in the study. Patients who met the recruitment criteria were randomly assigned into two groups of 24 each, labelled as propofol group (Group P) and dexmedetomidine group (Group D). Randomization was based on a computer generated random digits table. The patients recruited in the study were blinded to the group allocation.

On the day of the surgery, patients were shifted to operation theatre. Preinduction monitoring was started with five lead electrocardiogram, pulse oximetry, non invasive blood pressure and depth of anaesthesia was monitored with patient state index (PSI) and baseline values were recorded. An intravenous line was secured and intravenous fluid was started. After preoxygenation for 3-5 minutes general anaesthesia was induced with fentanyl (2 μg/kg) and propofol (titrated to loss of consciousness). After adequacy

of mask ventilation was ensured, vecuronium (0.1 mg/kg) was given. After 3 minutes, patients were intubated with appropriate size endotracheal tube via direct laryngoscopy/videolaryngoscopy/fibreoptic bronchoscopy based on patient's physiological or pathological considerations. Gas sampling was done through the side port attached to the ventilator circuit to monitor the end tidal carbon dioxide and anaesthetic gas levels. Invasive arterial line was inserted after induction, temperature probe was attached (body temperature was maintained throughout the procedure between 36-37 ^{0}C), and TOF (train of four) monitor was applied to stimulate median nerve on the normal side (unaffected side). Train of four stimulation was done to assess the degree of neuromuscular blockade and TOF ratio (ratio of amplitude of fourth twitch to first twitch) of 0.9 was taken as the starting point (T1) of the MEP monitoring.

MEP monitoring

Needle electrodes were placed over the scalp for electrical stimulation of motor cortex. MEPs were recorded from bilateral upper and/or lower extremities (according to the requirement of the case) using needle electrodes. The subdermal EEG needle electrodes used for the study purpose were 1.5 mm long and were of 27 G (Medtronic, Xomed). The equipment used for stimulating and recording MEP was Natus Neurology XLTEK brain monitor. The needle electrodes were placed after positioning and proper cleaning of the local site with chlorhexidine and 70% ethyl alcohol solution and then were secured using waterproof adhesive plasters.

A constant current electric stimulus of 70-200 mA (train of 9 pulses at 0.5 Hz) with interstimulus interval of 2-5 msec was applied transcranially to obtain a baseline waveform for MEP recording after attaining a TOF ratio of 0.9. The stimulus parameters

were kept the same as that used for obtaining the baseline for all the subsequent stimulations.

For placement of the stimulating electrodes 10-20 montage system was used. For recording MEP in the upper limb; stimulating electrodes were placed at C3 and C4 and MEP's were recorded in bilateral abductor pollicis brevis muscle (innervated by median nerve; C8, T1) using bipolar needle electrodes. For recording MEP in the lower limb; stimulating electrodes were placed at C1 and C2 and recorded in bilateral abductor hallucis muscle (innervated by medial plantar nerve; L4, L5) using bipolar needle electrodes. The distance between the two needle electrodes used for a single muscle recording was about 2 cm. The connecting wires for the electrodes were tied together to reduce the impedance. Electrodes inserted at C2 and C4 position were attached to the anode and those inserted at C1 and C3 were attached to the cathode. After getting MEP recordings from the left side the polarities of the electrodes were reversed to obtain recordings from the right side. The location of electrodes among these positions were dependent on the case requirement. This setting was used in both the groups.

Bite block was placed between the jaws. Ventilation was adjusted to obtain a stable airway pressure with end tidal carbon dioxide levels between 32 and 40 mm Hg (adjusted after obtaining an arterial blood gas to correlate with a partial pressure of carbon dioxide between 35 and 45 mm Hg). In all cases, the PSI was used to monitor the depth of anaesthesia, with the PSI maintained between 25 and 50 by titrating the level of the study drug (propofol or dexmedetomidine).

Heart rate, systolic, diastolic and mean arterial pressures, TOF and PSI values were recorded just after induction, after intubation, every 5 minutes for the first fifteen

minutes, every 15 minutes till first hour and then every 30 minutes till the end of the surgery to study the effect of the two modalities of anaesthesia on hemodynamics and depth of anaesthesia.

Just after induction anaesthesia was maintained with air and oxygen in 1:1 ratio, sevoflurane (MAC 0.4-0.5) and fentanyl infusion (1 µg/kg/hr) and either propofol or dexmedetomidine titrated to a PSI value of 25-50.

In Group P, propofol infusion was started just after induction at a rate of 75-100 µg/kg/min and titrated according to the PSI value (25-50).

In Group D, propofol infusion was started just after induction at a rate of 75-100 µg/kg/min and titrated according to the PSI value (25-50) till TOF ratio became

0.9 and continued for an additional 10 minutes. When TOF ratio was 0.9, dexmedetomidine loading dose was started at a rate of 0.5 µg/kg over 10 minutes. At the end of the loading dose, the propofol infusion was stopped and dexmedetomidine infusion was continued at a rate of 0.2-0.7 µg/kg/hr and titrated further according to the PSI value (25-50).

Amplitude (measured between the most positive and negative points of the CMAP in microvolts) and latency (measured between stimulus artefact and onset of response in milliseconds) of CMAP were recorded at the following points in both the groups –

T1–baseline value of MEP obtained when the TOF ratio reached 0.9, and before dividing the patients to two groups

T2 –10 min after T1 when the dexmedetomidine loading dose infusion would have just finished in Group D and in Group P 10 minutes past the point when TOF ratio reached 0.9

T3–10 minutes after T2

T4 – 10 minutes after T3

T5, T6 – recorded during the procedure

Tx – any other time if surgery requires it

Te – at the end of surgery

To study the effect of anaesthetic agents on the motor evoked potential waveforms the amplitude and latency of the waveforms were measured. More than 50% decrease in the amplitude and more than 10% prolongation of the latency of CMAP from the baseline values were defined as significant. Apart from that during the procedure if there was more than 80% decrease in amplitude of the waveforms, increase in threshold intensity, decrease in duration and complexity of the waveforms or complete disappearance of the waveforms, it was considered as an alarming situation and the surgeon was informed so that corrective measures could be taken up. Heart rate, systolic, mean and diastolic blood pressures and PSI and also the cumulative amount of the anaesthetic agents and opioids given till the time of each reading were also noted.

At the time of skin closure, the anaesthetic agents were stopped. The total amount of propofol, study drug and opioid required were recorded. Time taken for the return of spontaneous respiration, spontaneous movements, extubation, verbalization and to

regain orientation from the point of stopping the anaesthetic agents were also noted. Complications like bradycardia, tachycardia, hypertension, hypotension, unwanted limb movements or respiratory efforts, injury at the insertion site of electrodes, tongue laceration and intraoperative awareness were also recorded. Modified Brice questionnaire was used to detect intraoperative awareness. The questionnaire was used immediately after the patient was fully oriented to time, place and person, 24 hours and 7 days after the operation. The patients were classified as having definite/possible/no intraoperative awareness. Any new postoperative neurological deficits within 24 hours were also noted.

Bradycardia was defined as >20% drop in heart rate from the baseline or a value less than 60 bpm. Heart rate <50 bpm which lasted for >2 minutes was treated with intravenous atropine (0.5 mg) bolus administration. Tachycardia was defined as >20% increase in heart rate from baseline or a value >100 bpm. Hypotension, defined as a decrease of mean arterial pressure (MAP) >20% from the baseline, was treated using fluids/vasopressors, to maintain a constant MAP. Hypertension was defined as >20% increase in MAP from the baseline value. Consistent rise in heart rate and/or MAP lasting for >1 minute without any confounding factors (neural reflex, iatrogenic changes in blood pressure for checking hemostasis) was considered as pain stimulus and treated with 1 µg/kg (microgram per kilogram) bolus of fentanyl.

Statistical analysis

Motor evoked potentials generate two parameters which have a normal distribution in the population -

1. Amplitude

2. Latency

Based on a previous study by Yan et al (85), the difference in the means of the two parameters from the baseline in both the groups and their standard deviations were considered to calculate the sample size. More than 50% increase in amplitude from the baseline and more than 10% increase in latency from the baseline were considered as significant changes.

Table 1 -Calculation of sample size for the study

Trial parameters	latency	amplitude
Significance level, α	0.05	0.05
Power, 1-β	0.8	0.8
Difference in means	2.18	117
Standard deviation	2.6	140
Allocation ratio	1	1
One/Two sided	Two sided	Two sided
Total N	48	48

Thus, to get power of the study as 80%, sample size required was 48.

The baseline parameters and perioperative characteristics were analysed using the Student's T test (continuous variables) or the chi square test (qualitative variables).

Kolmogorov Smirnoff test was done to check whether the distribution of data was normal.

For comparing the amplitude and latency of the CMAP for a given group at T1, T2, T3, T4 and Te, repeated measures ANOVA with post hoc analysis and Bonferroni correction was used.

To compare the values of the amplitude and latency between the groups at different time points T test was used.

For comparing the hemodynamic parameters heart rate and MAP within a group at T1, T2, T3 and T4 repeated measures ANOVA with post hoc analysis and Bonferroni correction was used.

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

For comparing PSI values at different time intervals and recovery parameters between the groups T test was used.

To compare the rate of complications between the groups chi square test was used.

The software used for statistical analysis was IBM®SPSS statistics (version 26.0) software.

RESULTS AND OBSERVATION

We screened 58 patients fulfilling the inclusion criteria for the study. 48 patients completed the study. Five patients were excluded because of inability to obtain transcranial motor evoked potentials at all the required time points for the study. Four patients were excluded because neuromuscular relaxation was requested by the neurosurgeon. One patient was excluded because of SEDLINE PSI sensor failure. The recruitment and follow-up are detailed in the consort diagram as follows

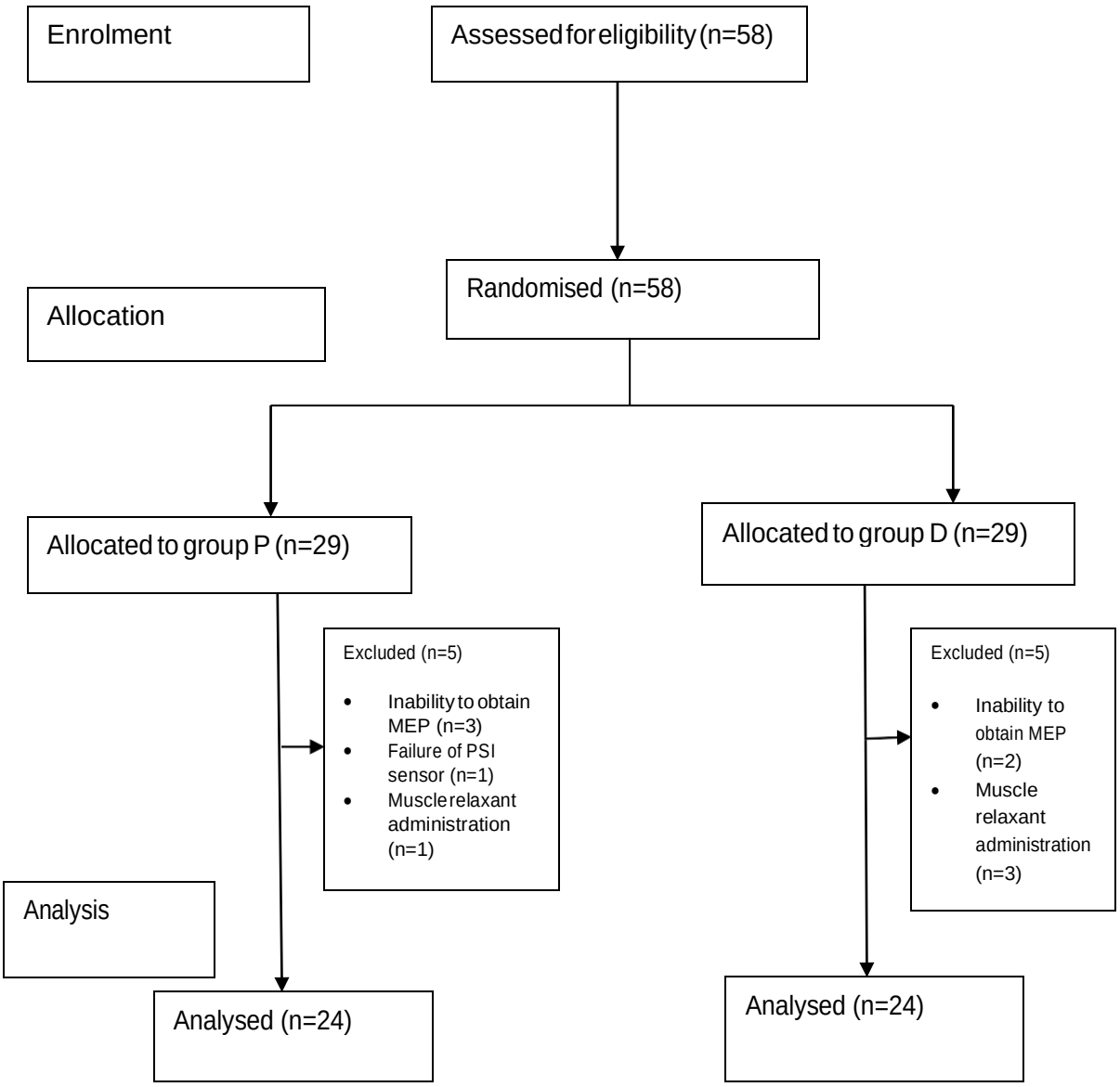

Figure 5 -Consort Diagram

Demographic data

The demographic parameters were comparable in both the groups as shown in Table 2.

Table 2 – Table comparing the demographic data between the two groups

Demographic characteristics		**Group P (n = 24)**	**Group D (n = 24)**	**P value**
Age in years (mean ± SD)		41.9 (14.1)	40.2 (12.8)	0.67
Weight in kg (mean ± SD)		62.8 (10.8)	62.8 (10.8)	1.00
Height in cm (mean ± SD)		160 (5.8)	161 (5.3)	0.85
Gender [male:female(%)]		11:13 (45.8:54.2)	11:13 (45.8:54.2)	1.00
ASA grade 1 (%)		9 (37.5)	11 (45.8)	0.56
ASA grade 2 (%)		15 (62.5)	13 (54.2)	
ASA grade 3/4/5 (%)		0 (0.0)	0 (0.0)	
Diagnosis	Cervical spine surgery (%)	14 (58.3)	12 (50.0)	0.40
	Thoracic spine surgery (%)	5 (20.8)	3 (12.5)	
	Lumbar/sacral spine surgery (%)	5 (20.8)	9 (37.5)	
Duration of surgery in min (mean±SD)		207.5 (39.4)	177.9 (64.9)	0.06
Duration of anaesthesia in min (mean±SD)		266.9 (38.0)	236.4(38.0)	0.06

Other perioperatve characteristics

Table 3 – Table comparing the motor power of the limbs and baseline current used to obtain MEP between the two groups

		Group P (n = 24)	**Group D (n = 24)**	**P value**
Motor power in RUL (%)	5	13 (54.2)	15 (62.5)	0.56
	4	11 (45.8)	9 (37.5)	
Motor power in LUL (%)	5	17 (70.8)	16 (66.7)	0.76
	4	7(29.2)	8 (33.3)	
Motor power in RLL (%)	5	19 (79.2)	20 (83.3)	0.71
	4	5 (20.8)	4 (16.7)	
Motor power in LLL (%)	5	19 (79.2)	21(87.5)	0.43
	4	5 (20.8)	3 (12.5)	
Current in mA (mean ± SD)		127.6 (23.4)	136.1 (23.8)	0.21

The distribution of power grading in all the limbs were comparable in both the sides between the groups as shown in Table 3. The baseline current for obtaining TcMEP was comparable in both the groups as shown in Table 3.

MEP recording

Amplitude

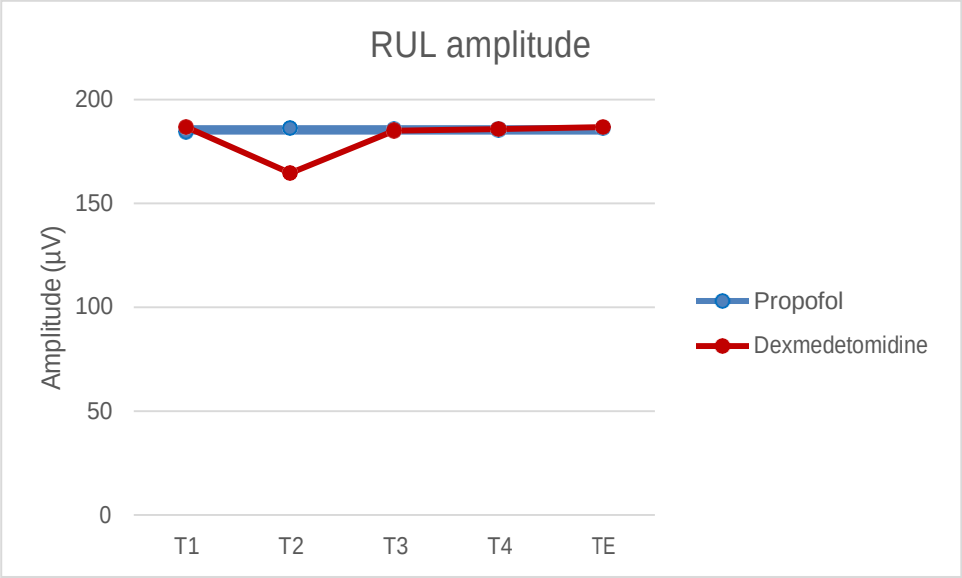

Figure 5 – Line diagram comparing the amplitude of CMAP obtained from right upper limb (RUL) between Group P and D

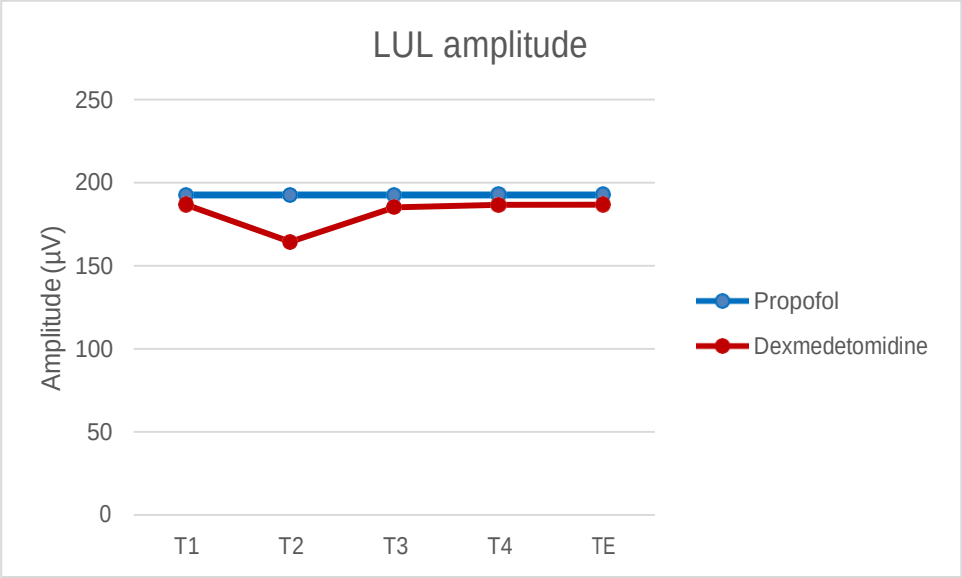

Figure 6 -Line diagram comparing the amplitude of CMAP obtained from left upper limb (LUL) between Group P and D

Table 4 – Table comparing the mean amplitude at T1, T2, T3, T4 and Te intergroup (T test) and intra group (repeated measures ANOVA) in upper limbs

RUL amp in µV	**T1 (mean ± SD)**	**T2 (mean ± SD)**	**T3 (mean ± SD)**	**T4 (mean ± SD)**	**Te (mean ± SD)**	**P value**
Group P (n=24)	184.6 (151.3)	186.3 (153.2)	185.6 (152.6)	185.5 (152.5)	186.2 (152.9)	0.17
Group D (n=24)	186.9 (79.4)	164.7 (69.0)*	185.1 (78.6)	185.9 (79.0)	186.8 (79.2)	<0.001*
P value	0.95	0.53	0.99	0.99	0.99	
LUL amp in µV						
Group P (n=24)	192.6(165.8)	192.4(165.8)	192.6(167.9)	192.8 (167.7)	192.9 (166)	0.38
Group D (n=24)	186.8(87.0)	164.4(75.7)*	185.1(82.3)	186.7(82.6)	186.8(82.4)	<0.001*
P value	0.88	0.45	0.84	0.87	0.87	

*significant ($p < 0.05$)

There was a significant difference between the amplitude values at T1 and T2 in both right and left upper limbs in Group Dwhereas there was no significant difference between the amplitude values at T1, T2, T3, T4 and Te of both right and left upper limbs in Group P (Figure 5, Figure 6; Table 4).

The mean values of amplitude at T1, T2, T3, T4 and Te for both right and left upper limbs were comparable between the groups (Figure 5, Figure 6; Table 4).

Lower limb MEP monitoring was done only in thoracic and lumbar cases, ie. 10 patients in Group P and 12 patients in Group D.

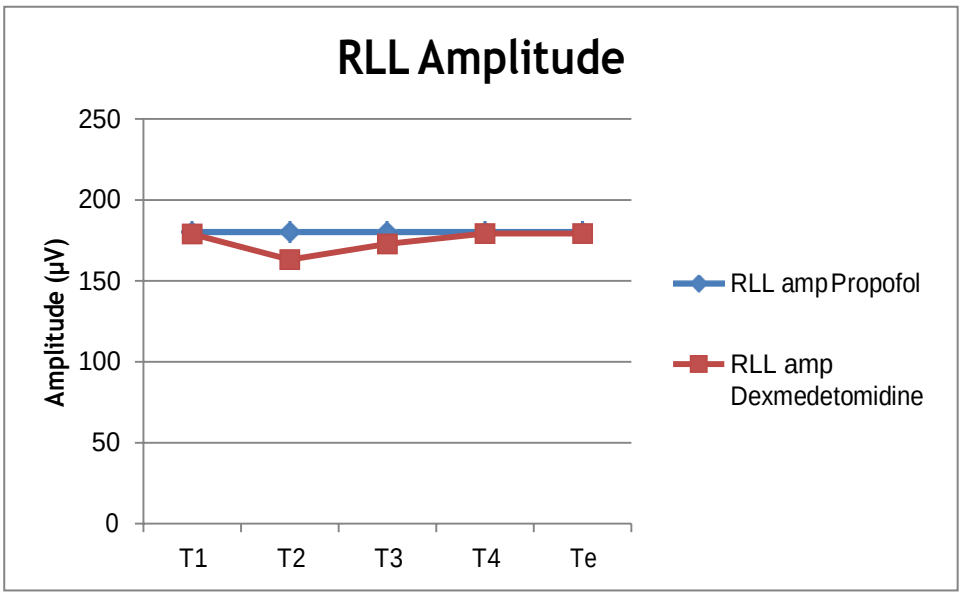

Figure 7 -Line diagram comparing the amplitude of CMAP obtained from right lower limb (RLL) between Group P and D

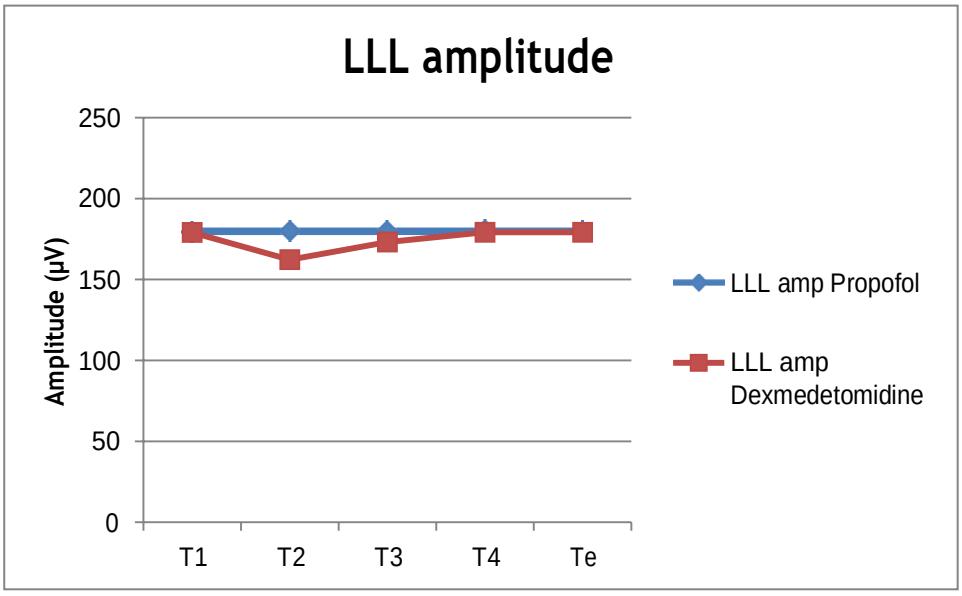

Figure 8 -Line diagram comparing the amplitude of CMAP obtained from left lower limb (LLL) between Group P and D

Table 5 – Table comparing the mean amplitude at T1, T2, T3, T4 and Te intergroup (T test) and intra group (repeated measures ANOVA) in lower limbs

RLL amp in µV	**T1 (mean ± SD)**	**T2 (mean ± SD)**	**T3 (mean ± SD)**	**T4 (mean ± SD)**	**Te (mean ± SD)**	**P value**
Group P (n=10)	180.2 (83.3)	180.2 (83.2)	180.2 (83.3)	180.3 (83.2)	180.1 (83.3)	0.11
Group D (n=12)	179.0 (63.8)	163.1 (65.8)*	172.8 (62.1)*	179.3 (63.6)	179.3 (64.0)	<0.001*
P value	0.97	0.60	0.81	0.97	0.98	
LLL amp in µV						
Group P (n=10)	179.4 (82.9)	180.1 (83.4)	180.2 (83.3)	180.4 (83.0)	180.1 (83.3)	0.45
Group D (n=12)	179.2 (63.2)	162.4(65.4)*	173.2(62.8)*	179.3 (63.6)	179.3 (64.0)	<0.001*
P value	0.10	0.58	0.83	0.97	0.98	

*significant ($p < 0.05$)

There was no significant difference between the amplitude values at T1, T2, T3, T4 and Te in both right and left lower limbs in Group P whereas in Group D the mean values at T2 and T3 were significantly lower than the mean values at T1 (Figure 7, Figure 8, Table 5).

The mean values of amplitude at T1, T2, T3, T4 and Te for both right and left lower limbs were comparable between the groups (Figure 7, Figure 8, Table 5).

Latency

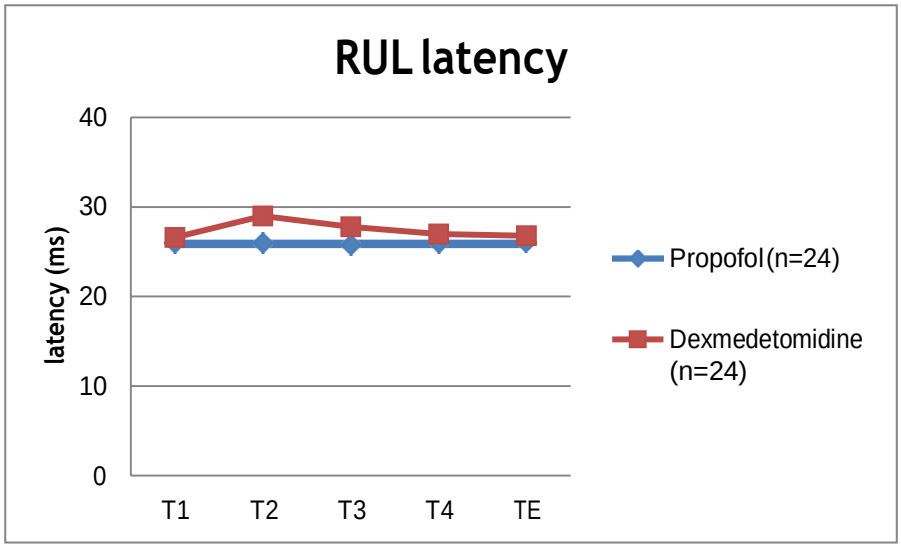

Figure 9 -Line diagram comparing the latency of CMAP obtained from right upper limb (RUL) between Group P and D

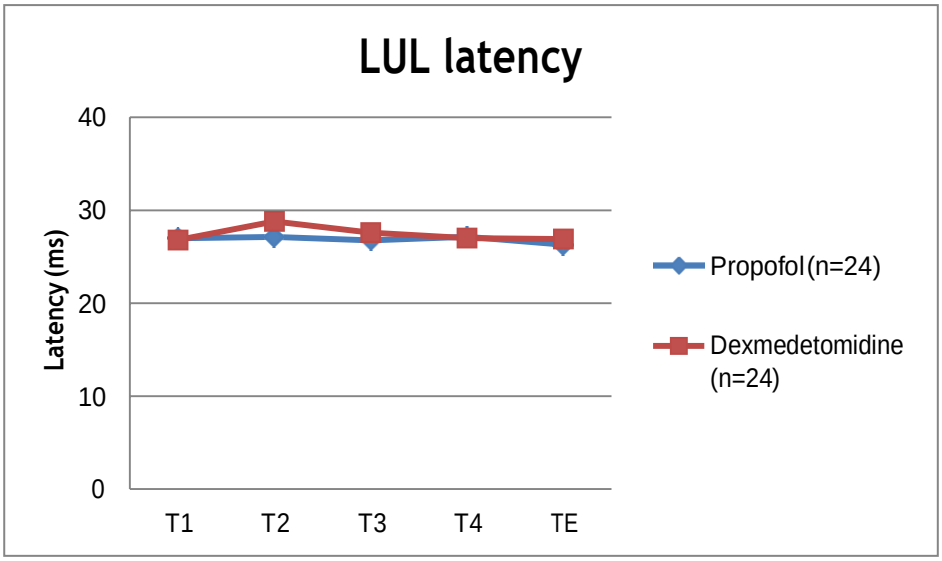

Figure 10 -Line diagram comparing the latency of CMAP obtained from left upper limb (LUL) between Group P and D

Table 6 – Table comparing the mean latency at T1, T2, T3, T4 and Te intergroup (T test) and intra group (repeated measures ANOVA) in upper limbs

RUL latency in ms	**T1 (mean ± SD)**	**T2 (mean ± SD)**	**T3 (mean ± SD)**	**T4 (mean ± SD)**	**Te (mean ± SD)**	**P value**
Group P (n=24)	25.9 (10.2)	27.1 (10.0)	26.8 (9.5)	27.2 (9.6)	26.3 (9.6)	0.47
Group D (n=24)	26.6 (4.4)	29(4.5)*	27.8(4.5)*	27.0 (4.4)	26.9(4.5)	<0.001*
P value	0.76	0.19	0.34	0.64	0.72	
LUL latency in ms						
Group P (n=24)	26.9(4.1)	27.1(4.2)	26.8(4.5)	26.9 (4.3)	26.3(4.8)	0.06
Group D (n=24)	26.8(4.1)	28.8(4.1)*	27.6(4.1)*	27.0 (4.2)	26.9(4.2)	<0.001*
P value	0.83	0.16	0.50	0.91	0.63	

*significant ($p < 0.05$)

There was no significant difference between the latency values at T1, T2, T3, T4 and Te in both upper limbs in Group P whereas in Group D it was found that the mean value at T2 and T3 were significantly higher than the mean values at T1 (Figure 9, Figure 10, Table 6).

The mean values at T1, T2, T3, T4 and Te for both right and left upper limbs were comparable between the groups (Figure 9, Figure 10, Table 6).

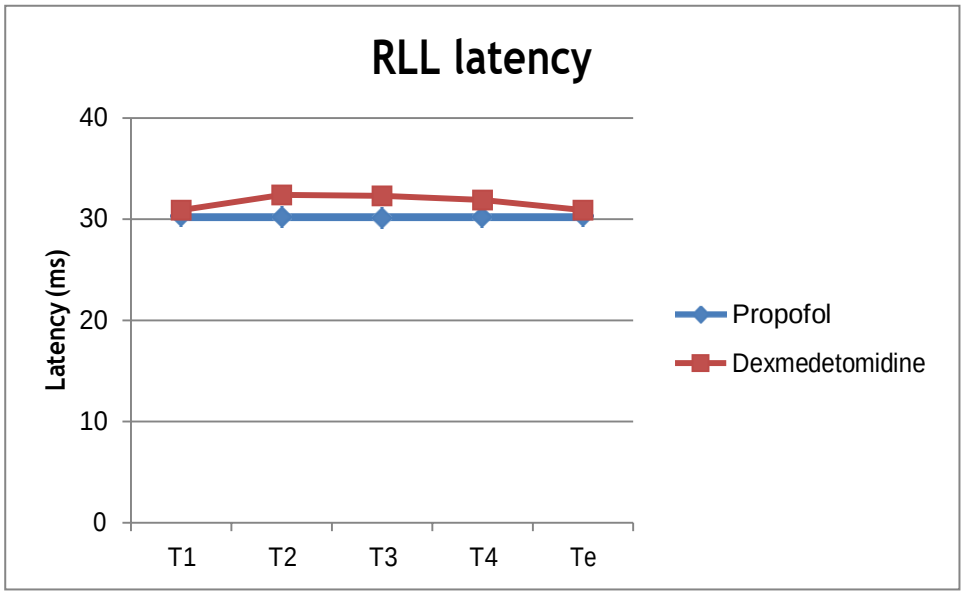

Figure 11 -Line diagram comparing the latency of CMAP obtained from right lower limb (RLL) between Group P and D

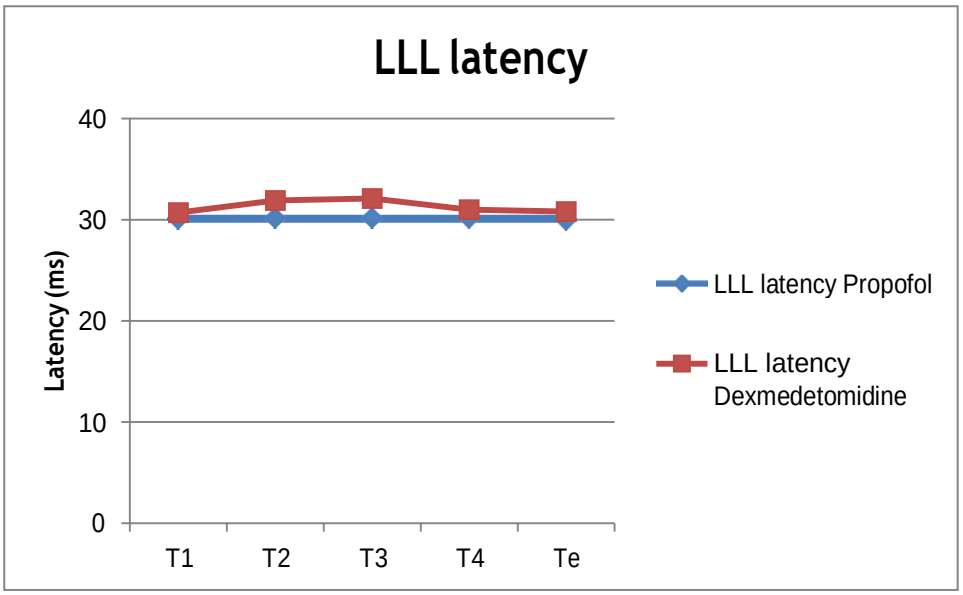

Figure 12 -Line diagram comparing the latency of CMAP obtained from left lower limb (LLL) between Group P and D

Table 7 – Table comparing the mean latency at T1, T2, T3, T4 and Te intergroup (T test) and intra group (repeated measures ANOVA) in lower limbs

RLL latency in ms	**T1 (mean ± SD)**	**T2 (mean ± SD)**	**T3 (mean ± SD)**	**T4 (mean ± SD)**	**Te (mean ± SD)**	**P value**
Group P (n=10)	30.3 (5.2)	30.2 (5.3)	30.1 (5.0)	30.2 (4.9)	30.3 (4.7)	0.87
Group D (n=12)	30.9 (7.3)	32.4 (6.6)*	32.3 (6.5)*	31.9 (6.5)*	30.9(6.9)	0.01*
P value	0.81	0.50	0.39	0.51	0.83	
LLL latency in ms						
Group P (n=10)	30.1 (5.0)	30.2 (4.9)	30.2 (5.1)	30.2 (4.9)	30.0 (5.0)	0.35
Group D (n=12)	30.7 (7.4)	31.9 (6.6)*	32.1 (6.4)*	31.0 (7.3)	30.8 (6.8)	0.002*
P value	0.82	0.50	0.45	0.78	0.76	

*significant ($p < 0.05$)

There was no significant difference between the latency values at T1, T2, T3, T4 and Te in right lower limb in Group P whereas in Group D it was found that the mean value at T2, T3 and T4 were significantly higher than the mean values at T1 (Figure 11, Figure 12, Table 7).

There was no significant difference between the latency values at T1, T2, T3, T4 and Te in left lower limb in Group P whereas in Group D it was found that the mean value at T2 and T3 were significantly higher than the mean values at T1 (Figure 11, Figure 12, Table 7).

The mean values at T1, T2, T3, T4 and Te for both right and left lower limbs were comparable in between the groups (Figure 11, Figure 12, Table 7).

In both right and left upper limb in Group D the average drop in amplitude at T2 was around 12% from baseline at T1. In right upper limb the average increase in latency at T2 and T3 was around 9% and 4.5% respectively from baseline at T1. In left upper limb in Group D, the average increase in latency at T2 and T3 was 7.4% and 2.9% respectively from the baseline at T1.

In right lower limb the average drop in amplitude at T2 and T3 was 8.8% and 2.6% respectively from baseline at T1. In left lower limb the average drop in amplitude at T2 and T3 was 9.3% and 3.3% respectively from baseline at T1. In right lower limb the average increase in latency at T2, T3 and T4 was 4.8%, 4.5% and 3.2% from baseline at T1. In left lower limb the average increase in latency at T2 and T3 was 3.9% and 4.5% respectively from baseline at T1.

None of these changes were clinically significant.

The dexmedetomidine loading dose given between point T1 and T2 titrated to PSI of 25-50 alongwith background fentanyl and propofol infusion and sevoflurane upto 0.5 MAC did not cause clinically significant changes in the MEP amplitude and latency in Group D.

Hemodynamic effects

Heart rate

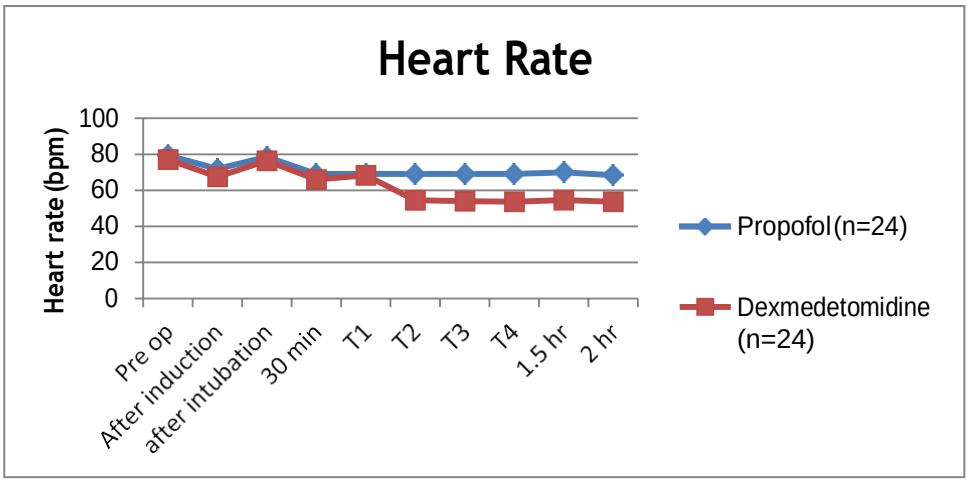

Figure 13 -Line diagram comparing the mean heart rate between Group P and D at different time interval

Table 7 – Table comparing the mean heart rate between the two groups at different time intervals

Heart rate (per min)	Group P (n = 24) Mean (SD)	Group P (n = 24) Mean (SD)	P value
Pre op	79.4 (17.2)	77.1(8.6)	0.56
After induction	71.9 (14.1)	67.6 (9.0)	0.21
After intubation	78.6 (15.4)	76.5 (9.1)	0.56
30 Min	69.1 (12.2)	66.0 (8.6)	0.31
T1	69.1(12.2)	68.4 (7.0)	0.81
T2	69.1(12.2)	54.5 (5.0)	<0.01*
T3	69.1 (12.2)	54.0 (4.9)	<0.01*
T4	69.1 (12.2)	53.7 (4.7)	<0.01*
1.5 Hr	70.0 (15.1)	54.6(4.9)	<0.01*
2 Hr	68.5 (11.7)	53.7 (4.2)	<0.01*

*significant ($p < 0.05$)

Table 8 – Table comparing the mean heart rate intragroup (repeated measures ANOVA) and between the two groups (T test) at T1, T2, T3 and T4

Heart rate (bpmin)	T1 (mean ± SD)	T2 (mean ± SD)	T3 (mean ± SD)	T4 (mean ± SD)	P value
Group P	69.1(12.2)	69.1(12.2)	69.1 (12.2)	69.1 (12.2)	0.00
Group D	68.4 (7.0)	54.5 (5.0)*	54.0 (4.9)*	53.7 (4.7)*	<0.001*
P value	0.81	<0.01*	<0.01*	<0.01*	

*significant ($p < 0.05$)

After starting dexmedetomidine (after T1), there was a significant drop in the heart rate in Group D as compared to Group P ($p < 0.01$) which was sustained throughout the infusion. (Figure 13, Table 7)

There was no significant difference between the mean heart rate at T1, T2, T3 and T4 in Group P. (Table 8)

In Group D heart rate was significantly lower at T2, T3 and T4 as compared to T1. (Table 8)

Mean arterial pressure

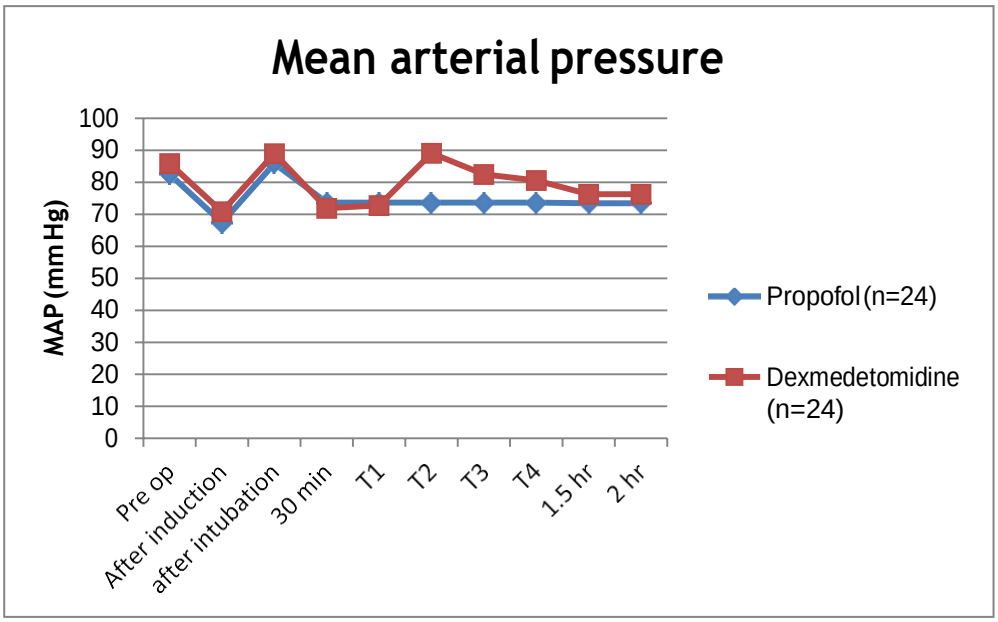

Figure 14 -Line diagram comparing the mean arterial blood pressure between Group P and D at different time intervals

Table 9 – Table comparing the mean arterial blood pressure between the two groups at different time intervals

MAP (mm Hg)	Group P(n = 24) Mean (SD)	Group D(n = 24) Mean (SD)	P value
Pre op	82.6(11.9)	85.9 (12.5)	0.36
After induction	67.4(7.1)	70.8(6.3)	0.08
After intubation	85.9(12.8)	89.0 (16.7)	0.47
30 Min	73.7(7.5)	71.9 (6.1)	0.38
T1	73.7 (7.5)	72.8 (4.7)	0.61
T2	73.7 (7.5)	89.1 (20.2)	0.001*
T3	73.7 (7.5)	82.5(15.0)	0.01*
T4	73.7(7.5)	80.6 (11.1)	0.01*
1.5 Hr	73.5 (3.7)	76.3 (8.8)	0.16
2 Hr	73.5 (3.7)	76.3 (8.8)	0.16

*significant ($p < 0.05$)

Table 10 – Table comparing the mean arterial blood pressure intragroup (repeated measures ANOVA) and between the two groups (T test) at T1, T2, T3 and T4

MAP (mm Hg)	T1 (mean ± SD)	T2 (mean ± SD)	T3 (mean ± SD)	T4 (mean ± SD)	P value
Group P (n=24)	73.7 (7.5)	73.7 (7.5)	73.7(7.5)	73.7 (7.5)	
Group D (n=24)	72.8 (4.7)	89.1(20.2)*	82.5 (15.0)*	80.6 (11.1)*	<0.001*
P value	0.61	0.001*	0.01*	0.01*	

*significant ($p < 0.05$)

There was no significant difference between the baseline values of the two groups. After starting dexmedetomidine in Group D, there was a significant increase in MAP at T2, T3 and T4 as compared to T1 which was more pronounced at T2 as compared to T3 and T4.(Figure 14, Table 9, Table 10)

Patient state index (PSI)

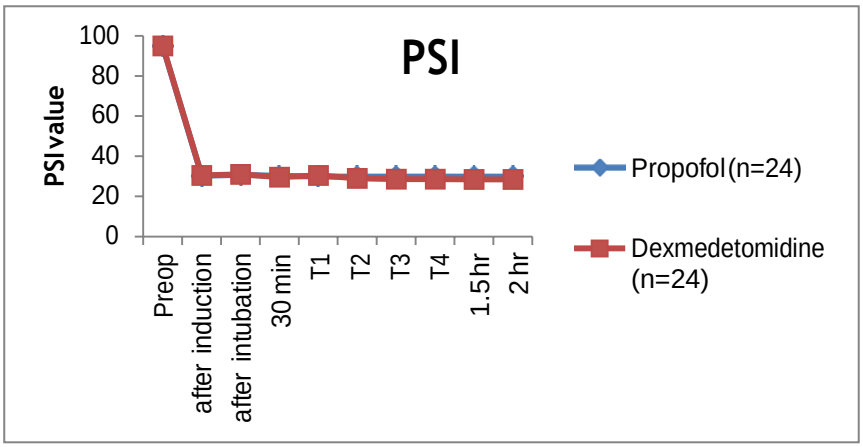

Figure 15 – Line diagram comparing PSI values between the groups at different time intervals

Table 11 – Table comparing the PSI values between the two groups at different time intervals

PSI	Group P(n = 24) Mean (SD)	Group D(n = 24) Mean (SD)	P value
Pre op	94.8 (4.3)	95.0 (2.7)	0.84
After induction	30.3(3.6)	30.5 (2.9)	0.79
After intubation	30.8 (3.1)	31.0 (2.6)	0.84
30 Min	30.3(3)	29.6(1.7)	0.32
T1	29.9(3.2)	30.5(2.2)	0.40
T2	29.9 (3.2)	29.0(2.2)	0.27
T3	29.9 (3.2)	28.6 (2)	0.10
T4	29.9 (3.2)	28.6 (1.9)	0.10
1.5 Hr	29.9(3.4)	28.5 (1.3)	0.10
2 Hr	29.9 (3.4)	28.5 (1.3)	0.10

There was no significant difference between the two groups in terms of PSI values throughout the operative period. (Figure 15, Table 11)

Rescue fentanyl

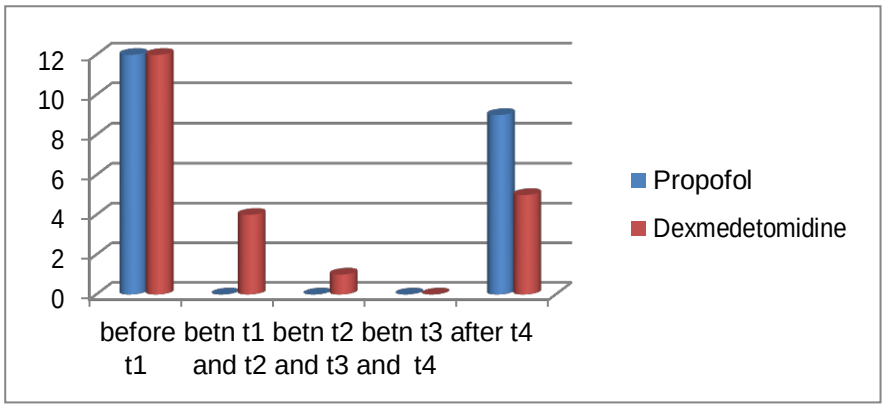

Figure 16 – Graph showing comparison of rescue fentanyl boluses at different time intervals between the groups

Table 12 – Table showing number of patients receiving fentanyl boluses at different time intervals between the groups

	Group P	**Group D**
Before T1	12	12
Between T1 and T2	0	4
Between T2 and T3	0	1
Between T3 and T4	0	0
After T4	9	5

The graph and the table denote the total number of patients who received fentanyl boluses (1 µg/kg) at different time intervals in each of the group. A continuous infusion of fentanyl was going on at a rate of 1 µg/kg/hr for all the patients in both the groups. 12 patients each in both the groups received fentanyl boluses before T1. Between T1 and T2, 4 patients received fentanyl boluses in group D and 1 patient was given fentanyl bolus between T2 and T3. None of the

patients received additional bolus in Group P between T1 and T4. After T4, 9 patients were given fentanyl boluses in Group P and 5 in Group D. (Figure 16, Table 12)

The average infusion dose of propofol used in group P was 5.6 (±1.23) mg/kg/hr (93.3 ± 20 µg/kg/min). The average loading dose of dexmedetomidine used in Group D was 0.5 µg/kg over 10 minutes and average maintenance dose used was 0.5 µg/kg/hr.

Recovery parameters

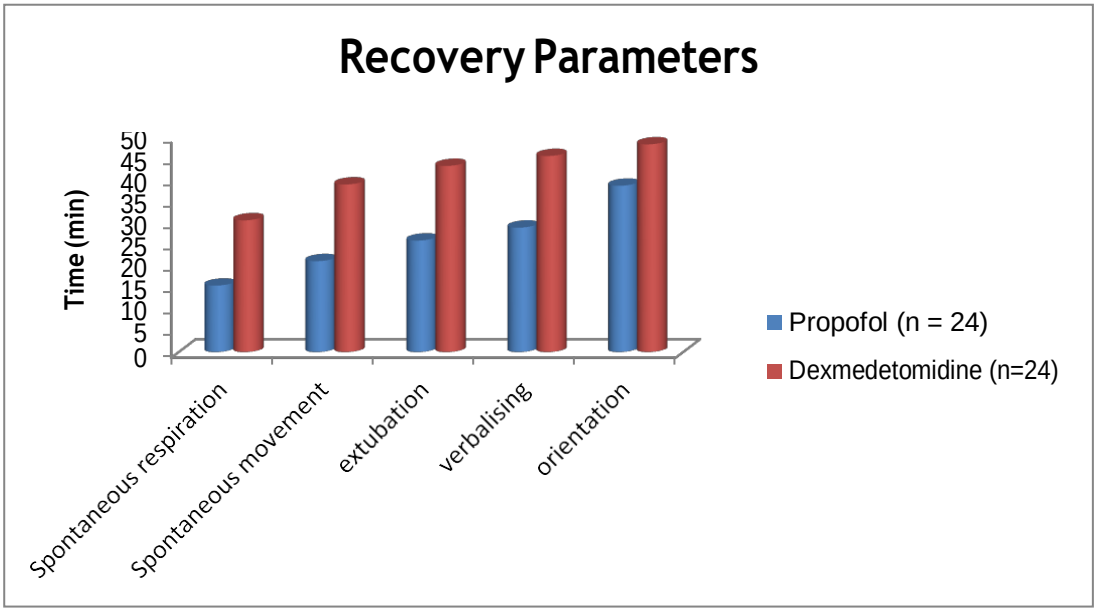

Figure 17 – Graph comparing the recovery parameters between the groups

Table 13 – Table showing comparison of the recovery parameters between the groups

Recovery parameters (min after stopping the anaesthetic agents)	**Group P(n = 24) Mean (SD)**	**Group D(n = 24) Mean (SD)**	**P value**
Spontaneous Respiration	15.5(5.5)	30.7(10.4)	p<0.01*
Spontaneous movement	21.2(6.9)	39.0(11.8)	p<0.01*
Extubation	26.0(8)	43.3(12.1)	p<0.01*
Verbalising	29.0(8.5)	45.6(13.6)	p<0.01*
Orientation	38.7(11.3)	48.3(14.5)	0.016*

*significant ($p < 0.05$)

There was a significant difference in the recovery parameters between both the groups. Time taken for patient to start breathing spontaneously, move limbs spontaneously, get extubated, start verbalising and get oriented to time, place and person were significantly prolonged in Group D. (Figure 17, Table 13)

Complications

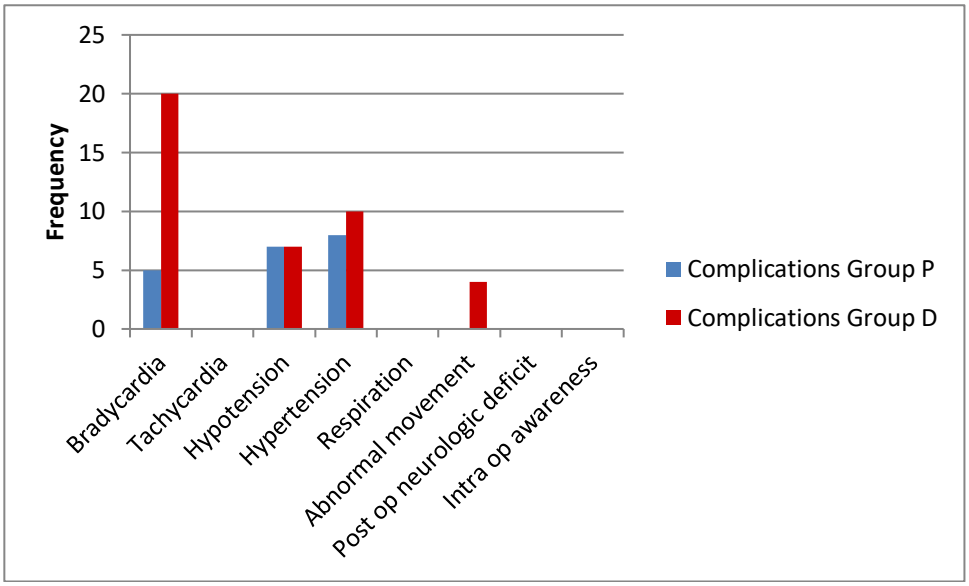

Figure 18 – Graph comparing the complications between the two groups

Table 14 – Table showing the complication rates between the two groups

Complications	**Group P (n = 24) (%)**	**Group D (n = 24)(%)**	**P value**
Bradycardia	5(20.8)	20(83.3)	0.003*
Hypotension (Hypo)	7(29.2)	7(29.2)	1.00
Hypertension (Hyper)	8(33.3)	10(41.7)	0.55
Abnormal movement	0(0.0)	4 (16.7)	0.038*

*significant ($p < 0.05$)

None of the patients in any group had tachycardia, tongue bite, local injury at pin insertion site, post operative neurological deficit or intraoperative awareness as determined by modified Brice questionnaire. The incidence of bradycardia and abnormal movements was significantly higher in Group D. (Figure 18, Table 14)

DISCUSSION

Motor evoked potential monitoring is being commonly used in neurosurgeries to assess the integrity of the motor tracts intraoperatively. Anaesthetic agents have an inhibitory effect on the synapses and thus most of the agents have a dose dependent inhibitory effect on MEP. If the doses of the anaesthetic agents are reduced to get an adequate MEP, there is a risk of intraoperative awareness. Therefore there is a need to use either a combination of anaesthetic agents or an adjuvant to reduce their inhibitory effect on MEP and at the same time provide adequate depth of anaesthesia during intraoperative MEP monitoring. The adjuvants should be able to have a sparing effect on the dose requirement of the anaesthetic agents as well have have an anaesthetic and analgesic effects of their own.

Both sevoflurane and propofol have a dose dependent depressive effect on TcMEP responses.

A study (64) suggests that propofol with effect site concentration of 2.5 µg/ml (50–75 µg/kg/min) and 0.5 MAC sevoflurane had comparable effects on MEP and reproduce reliable MEPs. But such low doses cannot produce an adequate depth of anaesthesia. Thus an adjuvant to these agents is required which will facilitate MEP and at the same time maintain an adequate depth of anaesthesia. And also an adjuvant to either low dose propofol or sevoflurane should have similar effects on MEP.

There are many studies which have evaluated the effects on MEP of dexmedetomidine as an adjuvant to low dose propofol (83, 85, 88 - 90) but similar studies with low dose sevoflurane are lacking.

In our study, we have evaluated the effects on MEP of dexmedetomidine as an adjuvant to low dose sevoflurane and compared it to the effects that a combination of propofol and low dose sevoflurane will have on MEP monitored during neurosurgeries. We have also compared the hemodynamic stability and recovery parameters and complications between the two anaesthetic regimens.

We recorded MEP bilaterally in all patients. Upper limb MEPs were recorded in all the study patients but lower limb MEPs were recorded in only 10 patients of Group P and 12 patients of Group D who underwent thoracic or lumbar spine surgeries. For the study purpose, comparison between the amplitude and latency of MEP obtained at four points T1, T2, T3 and T4, each of which was 10 minutes apart were taken before surgical stimulation of the spinal cord was done.

There was no significant difference noted between the two groups in terms of amplitude and latency at any given point of time. In Group P, after point T1 the same regimen was continued and no significant variations were noted among the subsequent readings. The addition of loading dose of dexmedetomidine in Group D caused a statistically significant decrease in amplitude and latency of MEP obtained at point T2 as compared to point T1. Amplitude starts recovering by the point T3 in Group D and the value at T4 is comparable to baseline T1. Latency also starts recovering by point T3 in Group D but still a statistically significant difference from the baseline was found in the latency values at point T3 in Group D. But by T4 the latency mean values were comparable to that of baseline in Group D.

The statistically significant decrease in amplitude and latency seen at T2 could be due to the combined effect of two drugs ie. propofol and dexmedetomidine loading dose. Mohamed et al had found a significant decrease in amplitude of MEP or complete disappearance of MEP after loading dose of dexmedetomidine in spine surgeries similar to our study but they had used a loading dose of 1 µg/kg with a background of propofol and remifentanil infusion. (97) In our study we used dexmedetomidine at a loading dose of 0.5 µg/kg with a background propofol infusion till point T1 and fentanyl at 1 µg/kg/hr with sevoflurane of 0.4 – 0.5 MAC.

Even though the changes in amplitude and latency were found statistically significant in Group D they were not clinically significant. Also the amplitude and latency were comparable between both the groups at any given point.

Similar to our findings, many studies had found that dexmedetomidine when used as an adjuvant did not depress the MEP response significantly. Li et al, Rozet et al, Tobias et al and Aschel et al have used dexmedetomidine as an adjuvant to propofol and had found that as compared to propofol alone there was no significant change in the amplitude or latency of the motor evoked potentials. (83, 85, 88 - 90)Bala et al studied the effects of dexmedetomidine as an adjuvant to 4% desflurane on MEP and had found that upto 0.6 ng/ml plasma concentration of dexmedetomidine did not have any significant effect on MEP amplitude and threshold current intensity. (84) All of the above mentioned studies have used a loading dose of 0.5 µg/kg of dexmedetomidine followed by an infusion of 0.5 µg/kg/hr similar to our study.

The PSI values in both the groups were comparable in our study. There are many studies that have used BIS/PSI to monitor depth of anaesthesia during dexmedetomidine infusion and have found a good correlation with other scales like Ramsay sedation score and Observer Assessment alertness/sedation score which reported good patient satisfaction score postoperatively. (95, 96) The dose of dexmedetomidine used in most of these studies was 0.5-1 µg/kg loading followed by 0.5 µg/kg/hr maintenance which was similar to our study. Also none of our patients had any awareness intraoperatively which was evaluated by the modified Brice questionnaire.

In our study it was seen that there was a significant decrease in the heart rate after starting the loading dose of dexmedetomidine in Group D. We also found that there was a significant rise in the mean arterial pressure after the loading dose of dexmedetomidine. The mean arterial pressure remained on the higher side even during the maintenance infusion as compared to Group P. After the loading dose of dexmedetomidine drop in heart rate with hypertension can be seen. (81) Hypertension is more common when the loading dose is given over ten minutes as in our case. It mostly occurs due to the intense vasoconstriction due to the stimulating effect of alpha-2 adrenoceptors. It can be avoided if the loading dose is given over a longer period. (81) This initial hypertension was also the reason for which according to our study protocol 5 patients received fentanyl boluses after point T2 without any actual rise in PSI values.

During the maintenance infusion of dexmedetomidine heart rate in Group D was significantly lower as compared to Group P. Also the mean arterial pressure in Group

D was higher than mean arterial pressure in Group P. Most of the studies have also found lower heart rate with dexmedetomidine as compared to propofol. In patients undergoing spinal tumour resection, Li et al had also found the heart rate to be significantly lower in the groups receiving propofol with dexmedetomidine as compared to propofol alone. They also found a higher mean arterial pressure in patients receiving both dexmdetomidine and propofol as compared to propofol alone. (85) Yan et al in his study on 84 patients who underwent general surgery found that dexmedetomidine in combination with propofol had higher incidence of hypertension and lower heart rates. (99) In most of the studies dexmedetomidine infusion was associated with lower heart rates despite the anaesthetic drug it was used with. (85 – 88, 99)

The amount of analgesic requirement in both the groups seemed equivalent. Between T1 and T4 points a significant rise in blood pressure was seen in group D after the loading dose of dexmedetomidine was given. To counter it fentanyl boluses were given but there was not any actual rise in PSI values and also there was no surgical stimuli between these two time points. If these boluses are excluded then it can be seen that after point T4 Group P had a greater analgesic requirement as compared to Group D. It can be because of analgesic property of dexmedetomidine which propofol lacks. Chakrabarti et al also found a lesser opioid requirement with dexmedetomidine and propofol combination as compared to propofol alone. (82)

In our study we found that the patients in Group D took significantly more time for extubation and getting oriented and verbalising as compared to Group P. This finding was in contrary to the findings in most of the studies which showed that

dexmedetomidine when used either alone or as an adjuvant to propofol did not alter the recovery parameters significantly. (85, 88, 100, 101) This could be due to the fact that the elimination half life of dexmedetomidine is around 2-3 hours and its context sensitive half time increases with increase in the infusion duration from 4 minutes after a 10 minutes duration to about 250 minutes after an 8 hour infusion. (102) In a study by Dong et al in orthopaedic procedures they found that even though there was a higher incidence of smooth emergence with better hemodynamic stability with a combination of sevoflurane and dexmedetomidine the recovery period (time to extubation) was significantly prolonged as compared to sevoflurane used alone and also the recovery period was prolonged when dexmedetomidine and propofol were used together as compared to propofol alone. (103) Laila et al also reported prolonged recovery time with dexmedetomidine used as a sole sedative agent during day care oral and maxillofacial surgeries. (104) It can be that dexmedetomidine used as an adjuvant can prolong the recovery period because of its sedative and analgesic action and a long context sensitive half life especially when used for long duration surgeries.

Incidence of bradycardia was significantly higher in Group D. These results were similar to that of Chakrabarti et al who compared propofol with a combination of dexmedetomidine and propofol. (82) There were 4 patients in group D that had an abnormal movement of limbs when the surgeon was working near the nerve roots. Complications like tongue injury, intraoperative respiratory efforts, needle site injury or intraoperative awareness were not seen in any of the patients. Abnormal movements can happen due to absence of muscle relaxation intraoperatively. Animal studies suggest that propofol has a muscle relaxant property by blocking sarcolemmal sodium

channels which can be a probable reason for none of the patients having any abnormal movements in Group P. (105)

LIMITATIONS

a) The study was done only in one institute in 48 patients. A larger multicentre trial is required to better understand its clinical applications.

b) The use of PSI, which evaluates depth of anaesthesia based on processed EEG cannot be justified completely for depth of anaesthesia monitoring in a dexmedetomidine based anaesthetic regimen even though previous studies have justified its use. We supplemented it with postoperative Modified Brice questionnaire to identify any potential intraoperative awareness in our study group. There was no incidence of intraoperative awareness in any of our patients.

c) Some of the patients in both the groups had weakness of variable duration (power of 4) in their limbs but their incidence was similar in both the groups. The differential effect of the anaesthetic regimens was not separately studied on the weaker limbs as compared to normal limbs.

d) In our study we used fentanyl as a rescue agent to treat hypertension induced by dexmedetomidine infusion which must have confounded our results of the analgesic requirement in both the groups.

CONCLUSION

A combined anaesthetic regimen of intravenous agents with low dose inhalational agents is commonly used to facilitate motor evoked potential monitoring intraoperatively. In our study we compared two such combined approaches – low dose sevoflurane with fentanyl infusion combination with propofol or dexmedetomidine. We concluded that

a) Dexmedetomidine can be used as an adjuvant to low dose sevoflurane and fentanyl for recording of adequate MEP responses. Even though the responses get depressed after the loading dose, it is not clinically significant and the responses (amplitude and latency) recover within 10 to 20 minutes and is comparable to baseline. It is preferable to finish the loading dose of dexmedetomidine before the start of surgery.
b) Dexmedetomidine infusion lowers the heart rate significantly. After the loading dose, it can cause an increase in mean arterial pressure. During dexmedetomidine infusion, the mean arterial pressures remain higher.
c) Patient's recovery from anaesthesia is prolonged when dexmedetomidine is used as an adjuvant to sevoflurane and fentanyl as compared to propofol.
d) Complications like bradycardia and abnormal limb movements are more common with dexmedetomidine as compared to propofol.

BIBLIOGRAPHY

1) Sutter M, Deletis V, Dvorak J, Eggspuehler A, Grob D, MacDonald D, et al. Current opinions and recommendations on multimodal intraoperative monitoring during spine surgeries. Eur Spine J. 2007; 16:232-7.

2) Legatt A D, Emerson R G, Epstein C M, MacDonald D B, Deletis V, Bravo R J, et al. ACNS Guideline: Transcranial Electrical Stimulation Motor Evoked Potential Monitoring. J Clin Neurophysiol. 2016; 33:42-50.

3) Deletis V. Basic methodological principles of multimodal intraoperative monitoring during spine surgeries. Eur Spine J. 2007; 16:147-52.

4) Chen Z. The effects of isoflurane and propofol on intraoperative neurophysiological monitoring during spinal surgery. J Clin Monit Comput. 2004; 18:303–8.

5) Scheufler KM, Reinacher PC, Blumrich W, Zentner J, Priebe HJ. The modifying effects of stimulation pattern and propofol plasma concentration on motor-evoked potentials. Anesth Analg. 2005; 100:440–7.

6) Mariappan R, Ashokkumar H, Kuppuswamy B. Comparing the effects of oral clonidine premedication with intraoperative dexmedetomidine infusion on anesthetic requirement and recovery from anesthesia in patients undergoing major spine surgery. J Neurosurg Anesthesiol. 2014; 26:192–7.

7) Freeman KA, Fullerton DA, Foley LS, Bell MT, Cleveland Jr JC, Weyant MJ, et al. Spinal cord protection in alpha-2 agonist-mediated increase in glial cell-line derived neurotropic factor. J Thorac Cardiovasc Surg. 2015; 149:578–86.

8) Raw D A, Beattie J K, Hunter J M. Anaesthesia for spinal surgery in adults. Br J Anaesth. 2003; 91:886-904.

9) Hadley M N, Shank C D, Rozzelle C J, Walters B C. Guidelines for the Use of Electrophysiological Monitoring for Surgery of the Human Spinal Column and Spinal Cord. Neurosurgery. 2017; 81:713–32.

10) Pelosi L, Lamb J, Grevitt M, Mehdian SM, Webb JK, Blumhardt LD. Combined monitoring of motor and somatosensory evoked potentials in orthopaedic spinal surgery. Clin neurophysiol. 2002; 113:1082-91.

11) Nuwer MR, Dawson EG, Carlson LG, Kanim LEA, Sherman JE. Somatosensory evoked potential spinal cord monitoring reduces neurologic deficits after scoliosis

surgery: results of a large multicenter survey. Electroencephalogr Clin Neurophysiol. 1995; 96:6-11.

12) Kothbauer K, Deletis V, Epstein FJ. Intraoperative spinal cord monitoring for intramedullary surgery: an essential adjunct. Pediatr Neurosurg. 1997; 26:247–54.

13) Kothbauer K, Deletis V, Epstein FJ, Motor evoked potential monitoring for intramedullary spinal cord tumor surgery. Neurosurg Focus. 1998; 4:1-9.

14) Sala F, Palandri G, Basso E, Lanteri P, Deletis V, Faccioli F, et al. Motor evoked potential monitoring improves outcome after surgery for intramedullary spinal cord tumors: a historical control study. Neurosurgery. 2006; 58:1129-43.

15) Deletis V, Sala F. Intraoperative neurophysiological monitoring of the spinal cord during spinal cord and spine surgery: A review focus on the corticospinal tracts. Clin Neurophysiol. 2008; 119: 248–64.

16) Jacobs MJ, Mess W, Mochtar B, Nijenhuis RJ, Statius RG, Schurink GW. The value of motor evoked potentials in reducing paraplegia during thoracoabdominal aneurysm repair. J Vasc Surg. 2006; 43:239-46.

17) Zho HH, Kelly PJ. Transcranial Electrical Motor Evoked Potential Monitoring for Brain Tumor Resection. Neurosurgery. 2001; 48:1075-81.

18) Szelenyi A, Camargo AB, Flamm E, Deletis V. Neurophysiological criteria for intra-operative prediction of pure motor hemiplegia during aneurysm surgery, J Neurosurg. 2003; 99:575–8.

19) Ichikawa T, Suzuki K, Sasaki T, Matsumoto M, Sakuma J, Oinuma M, et al. Utility and the limit of motor evoked potential monitoring for preventing complications in surgery for cerebral arteriovenous malformation. Neurosurgery. 2010; 67:222-8.

20) Sarnthein J, Bozinov O, Melone AG, Bertalanffy H. Motor-evoked potentials (MEP) during brainstem surgery to preserve corticospinal function. Acta neurochir. 2011; 153:1753-9.

21) Kawasaki Y, Uchida S, Onishi K, Toyokuni M, Okanari K, Fujiki M. Intraoperative Neurophysiologic Monitoring for Prediction of Postoperative

Neurological Improvement in a Child With Chiari Type I Malformation. J Craniofac Surg. 2017; 28:1837-41.

22) Stoelting R K, Rathmell J P, Flood P, Shafer S, Stoelting's handbook of Pharmacology and Physiology in Anesthetic Practice. 3rd ed. Philadelphia: Wolten Kluwer Pub. Co.; 2015. 46-55 p.

23) Penfield W, Rasmussen T. The cerebral cortex of man: a clinical study of localization of function. New York: Hafner Pub. Co.; 1968. 23-27 p.

24) Rose RD. Sensory component of cervically evoked motor potentials. Med Hypotheses. 1996; 46:577–9.

25) Minahan RE, Sepkuty JP, Lesser RP, Sponseller PD, Kostuik JP. Anterior spinal cord injury with preserved neurogenic 'motor' evoked potentials. Clin Neurophysiol. 2001; 112:1442–50.

26) MacDonald, Skinner S, Shils J, Yingling C. Intraoperative motor evoked potential monitoring – A position statement by the American Society of Neurophysiological Monitoring. Clin Neurophysiol. 2013; 124:2291–316.

27) Szelenyi A, Langer D, Beck J, Raabe A, Flamm ES, Seifert V, et al. Transcranial and direct cortical stimulation for motor evoked potential monitoring in intracerebral aneurysm surgery. Clin Neurophysiol. 2007; 37:391-8.

28) Barker AT, Freeston IL, Jalinous R, Jarratt JA. Magnetic stimulation of the human brain and peripheral nervous system: an introduction and the results of an initial clinical evaluation. Neurosurgery. 1987; 20:100–9.

29) Wrzosek M. Electroencephalography as a diagnostic technique for canine neurological diseases. J Vet Res. 2016; 60:181-7.

30) Legatt AD, Ellen R. Grass Lecture: Motor Evoked Potential Monitoring. Am J Electroneurodiagn Technol. 2004; 44:223-43.

31) Deletis V, Isgum V, Amassian V. Neurophysiological mechanisms underlying motor evoked potentials in anesthetized humans. Part 1. Recovery time of corticospinal tract direct waves elicited by pairs of transcranial electrical stimuli. Clin Neurophysiol. 2001; 112:438-44.

32) Ubags LH, Kalkman CJ, Been HD, Koelman JH, Ongerboer de Visser BW. A comparison of myogenic motor evoked responses to electrical and magnetic

transcranial stimulation during nitrous oxide/opioid anesthesia. Anesth Analg. 1999; 88:568–72.

33) Chipchase L, Schabrun S, Cohen L, Hodges P, Ridding M, Rothwell J, et al. A checklist for assessing the methodological quality of studies using transcranial magnetic stimulation to study the motor system: an international consensus study. Clin Neurophysiol. 2012; 123:1698–704.

34) Sloan T, Heyer EJ. Anesthesia for intraoperative neurophysiologic monitoring of the spinal cord. J Clin Neurophysiol. 2002; 19:430-43.

35) MacDonald DB, Dong CC. Spinal cord monitoring during descending aortic procedures. Handbook of Clinical Neurophysiology. 2008; 8:815-28.

36) Jameson LC, Sloan TB. Monitoring of the brain and spinal cord. Anesthesiol Clin. 2006; 24:777.

37) Calancie B, Harris W, Broton JG, Alexeeva N, Green BA. "Threshold-level" multipulse transcranial electrical stimulation of motor cortex for intraoperative monitoring of spinal motor tracts: description of method and comparison to somatosensory evoked potential monitoring. J Neurosurg. 1998; 88:457-70.

38) Langeloo DD, Journee HL, Kleuver M, Grotenhuis JA. Criteria for transcranial electrical motor evoked potential monitoring during spinal deformity surgery: A review and discussion of the literature. Neurophysiol Clin. 2007; 37:431-9.

39) MacDonald DB. Safety of Intraoperative Transcranial Electrical Stimulation Motor Evoked Potential Monitoring. J Clin Neurophysiol. 2002; 19:416–29.

40) Burke D, Hicks RG. Surgical monitoring of motor pathways. J Clin Neurophysiol. 1998; 15:194–205.

41) Calancie B, Harris W, Brindle GF, Green BA, Landy HJ. Threshold level repetitive transcranial electrical stimulation for intraoperative monitoring of central motor conduction. J Neurosurg Spine 1. 2001; 95:161–8.

42) Szelenyi A, Kothbauer KF, Deletis V. Transcranial electric stimulation for intraoperative motor evoked potential monitoring: Stimulation parameters and electrode montages. Clin Neurophysiol. 2007; 118:1586-95.

43) Oro J, Haghighi SS. Effects of altering core body temperature on somatosensory and motor evoked potentials in rats. Spine. 1992; 17:498-503.

44) Maylaerts SA, De Haan P. The effects of regional spinal cord hypothermia on transcranial myogenic motor evoked potential monitoring and the efficacy of spinal cord ischaemia detection. J Thorac Cardiovasc Surg. 1999; 118:1038-45.

45) Sakamoto T, Kawaguchi M. The effect of hypothermia on myogenic motor evoked potentials to an electrical stimulation with a single pulse and a train of pulses under propofol/ketamine/fentanyl anaesthesia in rabbits. Anaesth Analg. 2003; 96:1692-7.

46) Sueda T, Okada K. Evaluation of somatosensory and motor evoked potentials in thoracoabdominal aortic aneurysm surgery. Jpn J Thorac Cardiovasc Surg. 2000; 48: 60-5.

47) Leslie K, Sessler DI, Bjorksten AR, Moayyeri A. Mild hypothermia alters propofol pharmacokinetics and increases the duration of action of atracurium. Anesth Analg. 1995; 80:1007-14.

48) Haghighi SS, Keller BP, Oro JJ, Gibbs SR. Motor-evoked potential changes during hypoxic hypoxia. Surg neurol. 1993; 39:399-402.

49) Ataka H, Murakami M, Goto S, Moriya H, Hayashi F, Fukuda Y. Effects of hypoxia on the ventral root motor-evoked potential in the in vitro spinal cord preparation. Spine. 1996; 21:2095-100.

50) Short LH, Peterson RE, Monagan PD. Physiologic and anesthetic alterations on spinal-sciatic evoked responses in swine. Anesth Analg. 1993; 76:259–65.

51) Dolan EJ, Transfeld EE, Tator CH, Simmons EH, Hughes KF. The effects of spinal distraction on regional blood flow in cats. J Neurosurg. 1980; 53:756-64.

52) King BS, Rampil IJ. Anesthetic depression of spinal motor neurons may contribute to lack of movement in response to noxious stimuli. Anesthesiology. 1994; 81:1484–92.

53) Browning JL, Heizer ML, Baskin DS. Variations in corticomotor and somatosensory evoked potentials: effects of temperature, halothane anesthesia, and arterial partial pressure of CO2. Anesth Analg. 1992; 74:643–8.

54) Priori A, Berardelli A, Mercuri B, Inghilleri M, Manfredi M. The effect of hyperventilation on motor cortical inhibition in humans: a study of the electromyographic silent period evoked by transcranial brain stimulation. Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control. 1995; 97:69-72.

55) Hentschke H, Schwarz C. Antkowiak B. Neocortex is the major target of sedative concentrations of volatile anesthetics: Strong depression of firing rates and increase of GABAA receptor mediated inhibition. Eur J Neurosci. 2005; 21:93-102.

56) Burke, Bartley K. The effect of volatile anaesthetics on the excitability of human corticospinal tract. Brain. 2000; 123:992- 1000.

57) Sakamoto T, Kawaguchi M, Inoue S, Furuya H. Suppressive effect of nitrous oxide on motor evoked potentials can be reversed by train stimulation n rabbits under ketamine/ fentanyl anaesthesia, but not with additional propofol. Br J Anaesth. 2001; 86:395-402.

58) Haghighi SS, Sirintrapun SJ, Keller BP, Oro JJ, Madsen R. Effect of desflurane anesthesia on transcortical motor evoked potentials. J Neurosurg Anesthesiol. 1996; 8:47-51.

59) Ubags LH, Kalkman CJ, Been HD. Influence of isoflurane on myogenic motor evoked potentials to single and multiple transcranial stimuli during nitrous oxide/opioid anesthesia. Neurosurgery. 1998; 43:90–4.

60) Woodforth IJ, Hicks RG, Crawford MR, Stephen JP, Burke DJ. Variability of motor evoked potentials recorded during nitrous oxide anaesthesia from the tibialis anterior muscle after transcranial electrical stimulation. Anesth Analg. 1996; 82:744-9.

61) Zentner J, Albrecht T, Heuser D. Influence of halothane, enflurane, and isoflurane on motor evoked potentials. Neurosurgery. 1992; 31:298–305.

62) Pelosi L, Stevenson M, Hobbs GJ, Jardine A, Webb JK. Intraoperative motor evoked potentials to transcranial electrical stimulation during two anaesthetic regimens. Clin neurophysiol. 2001; 112:1076-87.

63) Chong CT, Manninen P, Sivanaser V, Subramanyam R, Lu N, Venkatraghavan L. Direct comparison of the effect of desflurane and sevoflurane on intraoperative motor-evoked potentials monitoring. J Neurosurg Anesthesiol. 2014; 26:306-12.

64) Hernandez-Palazon J, Izura V, Fuentes-Garcia D, Piqueras-Perez C, Domenech-Asensi P, Falcon-Arana L. Comparison of the Effects of Propofol and Sevoflurane Combined With Remifentanil on Transcranial Electric Motor-evoked and Somatosensory-evoked Potential Monitoring During Brainstem Surgery. J Neurosurg Anesthesiol. 2015; 27:282-88.

65) Martella G, De Persis C, Bonsi P, Natoli S, Cuomo D, Bernardi G, et al. Inhibition of persistent sodium current fraction and voltage-gated L-type calcium by propofol in cortical neurons: Implications for its antiepileptic activity. Epilepsia. 2005; 46:624-35.

66) Kakinohana M, Fuchigami T, Nakamura S, Kawabata T, Sugahara K. Propofol reduces spinal motor neuron excitability in humans. Anesth Analg. 2002; 94:1586–8.

67) Ubags LH, Kalkman CJ, Been HD, Drummond JC. Differential effects of nitrous oxide and propofol on myogenic transcranial motor evoked responses during sufentanil anaesthesia. Br J Anaesth. 1997; 79:590–4.

68) Van Dongen EP, Ter Beek HT, Aarts LP, Schepens MA, Morshuis WJ, Benning FJ,et al. The effect of two low-dose propofol infusions on the relationship between sixpulse transcranial electrical stimulation and the evoked lower extremity muscle response. Acta Anaesthesiol Scand. 2000; 44:799–803.

69) Kawaguchi M, Sakamoto T, Inoue S, Kakimoto M, Furuya H, Morimoto T, et al. Low-dose propofol as a supplement to ketamine-based anesthesia during intraoperative monitoring of motor-evoked potentials. Spine. 2000; 25:974–9.

70) Scheufler KM, Zentner J. Motor-evoked potential facilitation during progressive cortical suppression by propofol. Anesth Analg. 2002; 94:907–12.

71) Schonle PW, Isenberg C, Crozier TA, Dressler D, Machetanz J, Conrad B. Changes of transcranially evoked motor responses in man by midazolam, a short-acting benzodiazepine. Neurosci Lett. 1989; 101:321-4.

72) Aggarwal D, Mahajan HK, Chauhan PR. A comparative evaluation of dexmedetomidine with midazolam as an adjuvant to propofol anesthesia for spinal surgical procedures under motor evoked potential monitoring. Anaesth Pain & Intensive Care. 2016; 20:154-8.

73) Nadstawek J, Taniguchi M, Langenbach U, Thees C, Pechstein U, Schnitzler N. Effect of premedication and barbiturate hypnotics on motor evoked potentials induced by magnetic cortex stimulation. Anasthesiol Intensivmed Notfallmed Schmerzther. 1995; 30:361-5.

74) Kochs E, Treede RD, Schulte J. Increase in somatosensory evoked potentials during anesthesia induction with etomidate. Anaesthesist. 1986; 35:359-64.

75) Taniguchi M, Nadstawek J, Langenbach U, Bremer F, Schramm J. Effects of Four Intravenous Anesthetic Agents on Motor Evoked Potentials Elicited by Magnetic Transcranial Stimulation. Neurosurgery. 1993; 33:407–15.

76) Glassman SD, Shields CB, Linden RD, Zhang YP, Nixon AR, Johnson JR. Anesthetic effects on motor evoked potentials in dogs. Spine. 1993; 18:1083-9.

77) Yang LH, Lin SM, Lee WY, Liu CC. Intraoperative transcranial electrical motor evoked potential monitoring during spinal surgery under intravenous ketamine or etomidate anaesthesia. Acta Neurochir. 1994; 127:191-8.

78) Kalkman CJ, Drummond JC, Ribberink AA, Patel PM, Sano T, Bickford RG. Effects of propofol, etomidate, midazolam and fentanyl on motor evoked responses to transcranial electrical or magnetic stimulation in humans. Anesthesiology. 1992; 76:502-9.

79) Thees C, Scheufler KM, Nadastawek J, Pechstein U, Hanisch M, Juntke R, et al. Influence of fentanyl, alfentanil, and sufentanil on motor evoked potentials. J Neurosurg Anesthesiol. 1999; 11:112-8.

80) Kim W H, Lee J J, Lee S M, Park M N, Park S K, Seo D W, et al. Comparison of motor-evoked potentials monitoring in response to transcranial electrical stimulation in subjects undergoing neurosurgery with partial vs no neuromuscular block. Brit J Anaesth. 2013; 110: 567–76.

81) Miller R. Miller's anesthesia. 8th ed. Vol 1. Philadelphia:Elsevier; 2015. 855 – 860 p.

82) Chakrabarti D, Kamath S, Madhusudan Reddy KR, Srinivas DB, Manohar N, Masapu D. Effect of adjunctive dexmedetomidine on anesthesia and analgesia requirement and recovery characteristics during Bispectral Index-guided anesthesia for cerebello-pontine angle surgeries: A randomized clinical trial. J. Anaesthesiol Clin Pharmacol. 2018; 34:496-502.

83) Tobias JD. Dexmedetomidine:applications in pediatric critical care and pediatric anesthesiology. Pediatr Crit Care Med. 2007; 8:115-31.

84) Bala E, Sessler DI, Nair DR, McLain R, Dalton JE, Farag E. Motor and somatosensory evoked potentials are well maintained in patients given dexmedetomodine during spine surgery. Anesthesiology. 2008; 109:417-25.

85) Li Yan, Meng L, Peng Y, Qiao H, Guo L, Han R, et al. Effects of Dexmedetomidine on motor- and somatosensory-evoked potentials in patients with thoracic spinal cord tumor: a randomized controlled trial. BMC Anesthesiol. 2016; 16: 51.

86) Wei L, Deng X, Sui J, Wang L, Liu J. Dexmedetomidine Improves Intubating Conditions Without Muscle Relaxants in Children After Induction With Propofol and Remifentanil. Anesth Analg. 2015; 121:785-90.

87) Avidan M S, Zhang L, Burnside B, Finkel K J, Searleman A C, Selvidge J A, et al. Anesthesia Awareness and the Bispectral Index. N Engl J Med. 2008; 358:1097-108.

88) Anschel DJ, Aherne A, Soto RG, Carrion W, Hoegerl C, Nori P, et al. Successful intraoperative spinal cord monitoring during scoliosis surgery using a total intravenous anesthetic regimen including dexmedetomidine. J Clin Neurophysiol. 2008; 25:56–61.

89) Tobias JD, Goble TJ, Bates G, Anderson JT, Hoernschemeyer DG. Effects of dexmedetomidine on intraoperative motor and somatosensory evoked potential monitoring during spinal surgery in adolescents. Paediatr Anaesth. 2008; 18:1082–8.

90) Rozet I, Metzner J, Brown M, Treggiari MM, Slimp JC, Kinney G, et al. Dexmedetomidine does not affect evoked potentials during spine surgery. Anesth Analg. 2015; 121:492–501.

91) Lee KH, Kim YH, Sung YJ, Oh MK. The Patient State Index is well balanced for propofol sedation. Hippokratia. 2015; 19:235-8.

92) Drover D R, Lemmens H J, Pierce E T, Plourde G, Loyd G, Ornstein E, et al. Titration of Delivery and Recovery from Propofol, Alfentanil, and Nitrous Oxide Anesthesia. Anesthesiology. 2002; 97:82–9.

93) Soehle M, Keuch M, Grube M, Wirz S, Kruer S, Hoeft A, et al. Patient state index vs bispectral index as measures of the electroencephalographic effects of propofol. Brit J Anaes. 2010; 105:172-8.

94) Prichep L S, Gugino L D, John E R, Chabot R, Howard B, Merkin H, et al. The Patient State Index as an indicator of the level of hypnosis under general anaesthesia. Brit J Anaesth. 2004; 92: 393-9.

95) Park S, Choi JH, Kim HT, Cho Y. Replacement of dexmedetomidine loading with midazolam for sedation in elderly patients with spinal anesthesia. Medicine. 2018; 97:e12565.

96) Sayed E, Yassen KA. Intraoperative effect of dexmedetomidine infusion during living donor liver transplantation: A randomized control trial. Saudi J Anaesth. 2016; 10:288-94.

97) Mahmoud M, Sadhasivam S, Sestokas AK, Samuels P, McAuliffe J. Loss of transcranial electric motor evoked potentials during pediatric spine surgery. Anesthesiology. 2007; 106:393-6.

98) Mahmoud M, Sadhasivam S, Salisbury S, Nick T G, Schnell B, Sestokas A K, et al. Susceptibility of Transcranial Electric Motor-evoked Potentials to Varying Targeted Blood Levels of Dexmedetomidine during Spine Surgery. Anesthesiology. 2010; 112:1364 –73.

99) Han Y, Han L, Dong M, Sun Q, Ding K, Zhang Z, et al. Comparison of a loading dose of dexmedetomidine combined with propofol or sevoflurane for hemodynamic changes during anesthesia maintenance: a prospective, randomized, double-blind, controlled clinical trial. BMC Anesthesiol. 2018; 18:12.

100) Srivastava VK, Agrawal S, Kumar S, Khan S, Sharma S, Kumar R. Comparative Evaluation of Dexmedetomidine and Propofol Along With Scalp Block on Haemodynamic and Postoperative Recovery for Chronic Subdural Haematoma Evacuation Under Monitored Anaesthesia Care. Turk J Anaesthesiol Reanim. 2018; 46:51–6.

101) Bharathwaj D K, Kamath S S. Comparison of dexmedetomidine versus propofol-based anaesthesia for controlled hypotension in functional endoscopic sinus surgery. South Afr J Anaesth Analg. 2018; 0:1–4.

102) Venn RM, Karol MD, Grounds RM. Pharmacokinetics of dexmedetomidine infusions for sedation of postoperative patients requiring intensive care. Br J Anaesth. 2002; 88:669-75.

103) Kim DJ, Kim SH, So KY, Jung KT. Effects of dexmedetomidine on smooth emergence from anaesthesia in elderly patients undergoing orthopaedic surgery. BMC Anesthesiol. 2015; 15:139.

104) Makary L, Vornik V, Finn R, Lenkovsky F, Mcclelland AL, Thurmon J, et al. Prolonged Recovery Associated With Dexmedetomidine When Used as a Sole Sedative Agent in Office-Based Oral and Maxillofacial Surgery Procedures. J Oral Maxillofac Surg. 2010; 68:386-91.

105) Haeseler G, Stormer M, Bufler J, Dengler R, Hecker H, Piepenbrock S, et al. Propofol blocks human skeletal muscle sodium channels in a voltage-dependent manner. Anesth Analg. 2001; 92:1192-8.

ANNEXURES

ANNEXURE 1

Proforma

Name

Hospital number

Age

Sex if female-pregnant/nursing

Diagnosis

	yes	no
Informed consent		
Autonomic instability		
Neurological/neuromuscular disease		
Cardiac/pulmonary/renal/hepatic disease		
Skull defects/injury at local site of needle electrode insertion		
Diabetes(if yes specify duration)		
Alcohol use (if yes specify duration)		
Allergy to anesthetic agents		

Proposed surgery

Other specifications -

Preoperative parameters

	Heart rate	Blood pressure	Saturation
In ward/icu			
In ot before induction			

Hemodynamics

	Heart rate	MAP	Saturation	PSI	TOF
After induction					
After intubation					
10 min					
20 min					
30 min					
45 min					
1 hr					
1.5 hr					
2 hr					
2.5 hr					
3 hr					
3.5 hr					
4 hr					
4.5 hr					
5 hr					

Amount of drugs used intraoperatively –

Duration	Study drug	Fentanyl	Sevoflurane	Propofol	Rescue (fentanyl)
1st hr					
2nd hr					
3rd hr					
4th hr					
5th hr					

When T4/T1 ≥ 0.9

	Heart rate	MAP	Saturation	$EtCO_2$	PSI	TOF	Cumulative dose of study drug	Cumulative dose of fentanyl	Cumulative dose of propofol
T1									
T2									
T3									
T4									
T5									
T6									
Tx1									
Tx2									
Te									

MEP

	Left UL		Left LL		Right UL		Right LL	
	Amplitude	Latency	Amplitude	Latency	Amplitude	Latency	Amplitude	Latency
T1								
T2								
T3								
T4								
T5								
T6								
Tx1								
Tx2								
Te								

Recovery

	Time (min) – after stopping anaesthetic agents
Respiration	
Spontaneous movements	
Extubation	
Verbal	
Cooperation	
orientation	
ICU discharge	

Any post operative complications –

Complications	Frequency
Bradycardia	
Tachycardia	
Hypertension	
Hypotension	
Respiratory efforts	
Any movement	
Tongue bite	
Any other injury	
Intraoperative awareness	

ANNEXURE 2

Modified Brice Questionnaire

Were you expecting to be completely asleep for this operation (please circle)? YES / NO

1. What is the last thing you remember before going to sleep (please tick one box)?

-Being in the pre-op area ☐ -Seeing the operating room ☐

-Being with family ☐ -Hearing voices ☐

-Feeling mask on face ☐ -Smell of gas ☐

-Burning or stinging in the IV line ☐ -Other [Please write below]:

_____

2. What is the first thing you remember after waking up (please tick one box)?

-Hearing voices ☐ -Feeling breathing tube ☐

-Feeling mask on face ☐ -Feeling pain ☐

-Seeing the operating room ☐ -Being in the recovery room ☐

-Being with family ☐ -Being in ICU ☐

-Nothing ☐ -Other [Please write below]:

_____

3. Do you remember anything between going to sleep and waking up (please tick box)?

-No ☐

-Yes: -Hearing voices ☐ -Hearing events of the surgery ☐

-Unable to move or breathe ☐ -Anxiety/stress ☐

-Feeling pain ☐ -Sensation of breathing tube ☐

-Feeling surgery without pain ☐ -Other [Please write below]

_____

4. Did you dream during your procedure (please tick box)?

-No ☐ -Yes ☐

-What about [Please write below]:

_____

5. Were your dreams disturbing to you (please tick box)?

-No □ -Yes □

6. What was the worst thing about your operation (please tick box)?

-Anxiety □ -Pain □

-Recovery process ☐ -Unable to carry out usual activities ☐

-Awareness ☐ -Other [Please write below]:

_____

ANNEXURE 3

PATIENT INFORMATION FORM

Title of the study:

Comparison of effects of propofol and dexmedetomidine on motor evoked potentials in neurosurgery.

Name of the Investigators:

Dr. Soniya Biswas, Dr. Smita V., Dr. Unnikrishnan P.

You are being requested to participate in this study which compares the effects of propofol and dexmedetomidine on motor evoked potentials in neurosurgery. We have planned to include about people from this hospital in this study.

What is motor evoked potential and does it have any side effects?

Motor-evoked potential (MEP) is widely used during neuro surgeries**.** The MEP is produced by electrical stimulation of a part of a brain using scalp electrodes. After stimulation, the activity of the muscles of both arms and legs which gets activated after the stimulation is recorded using another set of electrodes. As you will be under anesthesia, you will not be aware of this stimulation and you will also not feel any pain. Sometimes after stimulation there can be some movement of tongue which will be protected using a bite block so that there is no injury. The electrodes which are inserted in the arms and legs are minute sized pins. They will be not cause any pain as you will be under anesthesia and their size is so small that they will also not cause any injury at the insertion site. The length of the pins is also less so that they will not go very deep inside. The pin insertion sites will be kept nicely padded.

What is propofol and does it have any side effects?

Propofol is a sedative drug which is given through vein. It is approved for use in neuroanaesthesia and being used worldwide including our institute. It will be discontinued after surgery and you will recover from anesthesia. It can cause decrease in blood pressure but we will use it at a rate which will cause this side effect. It can cause stinging sensation in vein while injection. We will prevent it by giving low dose of another drug lignocaine.

What is dexmedetomidine and does it have any side effects?

Dexmedetomidine is a sedative drug which is given through vein. Along with the property of inducing sleep it reduces pain and vomiting. It is approved for use in neuroanaesthesia and being used worldwide including our institute. It will be discontinued after surgery and you will recover from anesthesia. Dexmedetomidine in higher doses (> 0.8 mcg/Kg/hour) reduces the heart rate and blood pressure. However the dose we are using does not have any adverse effects according to available literature in scientific journals.

If you take part what will you have to do?

You will be included in the study only if you are willing. On the day of surgery you will be anaesthetized according to the standard protocol of our institute and breathing tube will be placed for giving artificial breathing. Our study will start after induction. Electrodes will be placed on your scalp and all the four limbs to monitor motor evoked potentials.To maintain

anaesthesia during surgery you will be administered anesthetic gases or drugs through vein. You will be allotted to any one of the two groups:

First group will receive propofol till the end of surgery

Second group will receive propofol for sometime and then dexmedetomidine

Please note that there is no advantage of any of the techniques over another for maintenance of anesthesia. Both are equally safe and effective. The study purpose is only to record the effect of these drugs on motor evoked potentials. The quality of surgery will not be affected by the difference in the anesthesia techniques.

The motor evoked potentials will be recorded at different time intervals during the surgery. You will not feel any pain or become aware during the recordings. After the end of surgical procedure the drugs will be stopped.

You will be asked to open your eyes, make hand grip and if they are adequate the breathing tube will be taken out. Then you will be asked about time, place and date to assess your recovery from anesthesia.You will be asked about any complaints which will be taken care of. After that you will be shifted to ICU where postsurgery care will be taken up.

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.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you since the anaesthesia technique and monitoring tools would be same even if you were not part of the study. In addition, adverse events related to motor evoked potential monitoring is minimal. But ***if you do develop any side effects or problems due to the study, the side effects will be treated at no cost to you. We are unable to provide any monetary compensation, however***.

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

Motor evoked potential monitor is used as a part of anaesthesia procedures for surgery. So, no extra money will be charged from the patients.

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. Soniya Biswas (Principal investigator) mobile number: 9336693999. Email: soniyabiswas2103@gmail.com.

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

CONSENT FORM

Participant's name: **Date of Birth / 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 effects of propofol and dexmedetomidine on motor evoked potentials in 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:

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Xm¦Ä]T\¯nsâ `mKasÃ¦nepw ab¡m\pÅ kt¦X§fpw \nco£W kwhn[m\hpw H¶pXs¶bmsW¶Xn\mÂ ]T\kw_ÔnbmbnXm¦Ä¡]cp¡pIsfm¶pw R§Ä {]Xo£n¡p¶nÃ. tamt«mÀ CthmIUv s]m«³jyepambn _Ôs¸« tZmjIcamb kw`h§fpw hfsc IpdhmWv.]t£]T\hpambn _Ôs¸« Xm¦Äs¡s´¦nepw]mÀiz^e§tfm {]i\§tfm D—mbmÂ Ah Xm¦Ä¡A[nINnehp—mImsX NnInÕn¡s¸Spw. F¶ncp ¶nepw km¼¯nIamb \jvS]cnlmcw \ÂIm³ R§Ä¡mhnÃ.

D]IcW§fp]tbmKn¡p¶Xnsâ Nneh Xm¦Ä \ÂIWtam?

tamt«mÀ CthmIUv s]m«³jyÂ \nco£Ww ik{X{Inb¡pth—nbpÅ ab¡ensâ `mK ambn D]tbmKn¡p¶XmWv. BIbmÂ tcmKnbnÂ \n¶pw A[nI Nneshm¶pw CuSm¡nÃ.

Xm¦fpsS hyànKXhnhc§Ä cIkyambncn¡ptam

]T\¯nsâ `mKambpÅ KthjW{]_Ô kaÀ¸W¯n\ Cu]T\¯nse ^e§Ä D]tbmKn¡pw, Hcp sshZyimkv{X {]kn²oIcW¯n\ \ÂIpw,]t£ Xm¦sf hyànKXambn t]cpsImv Xncn¨dnbm\pXIp¶sXm¶pw]T\^e¯nsâ {]ZÀi\¯ntem {]kn²oIcW¯ntem D-mhnÃ. F¶ncp¶nepw, Xm¦Ä]T\¯nÂ]s¦Sp¡m³ Xocpam\n¨mÂ Xm¦fpsS NnInÕm tcJIÄ]T\hpambn _Ôs¸«bmfpIÄ Xm¦fpsS {]tXyI A\paXnbn ÃmsX]cntim[nt¨¡mw.

Xm¦Ä¡IpSpXses´¦nepw tNmZy§fps—¦nÂ Zbhmbn tUm. tkmWnb _nizmkn ({][m\ KthjI) s\ _Ôs¸SpI. samss_Â \¼À. 9336693999, CsabnÂ. soniyabiswas2103@gmail.com.

sSI\n¡Â AssUzkdn I½näp¡mbn Zbhmbn _Ôs¸SpI. tUm amem cma\mY³ t^m¬ \¼À. 0471þ2524234. CsabnÂ. iec.mem.sec@sctimst.ac.in

k½X]{Xw

]T\ ioÀjIw. \yqtdm ikv{X{InbbnÂ tamt«mÀ C³thmIU s]m«³jyÂ F¶ \ncoEW kwhn[m\ ¯nÂ s{]mS¸mt^mÄ, UIkvsaUntämanssU³ F¶nhbpsS {]`mh¯nsâ Xmc Xayw.

Kthj Icps S t]c. tUm. tkmWnb _nizmk, tUm kanX hn, tUm D®nIrjW³]n

]s¦Sp¯p¶bmfpsS t]cv ……..

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{]kvXmhn¯p¶p. (Zbhmbn t_mIvknÀ SnIv ( ) sN¿pI

- \yqtdm ikv{X{InbbnÂ t]inIsf Nen¸n¡p¶ akvXnjv¯`mKs¯ {]tNmZn¸n¯p¶Xnsâ km²yXIfnÂ s{]mS¸mt^mÄ UIkvsaUntämanssU³ F¶nhbpsS {]`mh¯nsâ Xmc Xayw F¶]T\kw_ÔnbmbnF\n¡v apIfnÂ X¶ hnhc§Ä hmbn¨p.[]
- F\n¯p—mb kwib§Ä]cnIcn¨p. []
- Fsâ Cu]T\¯nepÅ]¦mf¯w kzta[bmbpÅXmsW¶pw]T\¯nÂ XpScp¶Xn \pÅ A\phmZw GXpkab¯pw Fsâ km[mcWbmbpÅ NnInÕsbtbm \nba]camb AhImi§sfsbm _m[n¯msX F\n¡n³henm\mIpsa¶pw a\ÊnemIp¶p. []
- Rm³ Cu]T\¯nÂ \n¶pw]n³amdnbmepw Fsâ NnInÕmtcJIÄ KthjWw \S¯p¶ hÀtim Ømn\¯nse ss\XoII½näm AwK§Ätim]cntim[n¡m³ Fsâ k½Xw Bhiyan sÃ¶p Rm³ a\ÊnemIp¶p. AXn\\phZnIp¶p. []
- aq¶mw I£nIÄtim {]kn²oIcW¯ntem Fsâ hyàn hnhc§Ä ssIamdnsÃ¶pw Rm³ a\ÊnemIp¶p. []
- Rm³ kzta[bm]T\¯nÂ]s¦Sp¡m³ k½XnIp¶p. []
- F\n¡v]T\s¯¸äntbm]s¦SpIp¶p¶bmfpsS AhImi§sf¸äntbm IpSpXednbWsa ¦nÂ {][m\Kthj Isb _Ôs¸Sm³ \¼À X¶n«p—[]
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t]c

H¸ XobXn

From:
Dr. Soniya Biswas
Senior resident,
Neuroanesthesiology division,
Department of anaesthesiology,
SCTIMST,
Thiruvananthapuram

To,
The Chairman,
Institutional Ethics Committee
SCTIMST,
Thiruvananthapuram

Respected Sir/Madam

Subject – Request for change in study proposal title (IEC/1152)

My study proposal titled "COMPARISON OF EFFECTS OF PROPOFOL AND DEXMEDETOMIDINE ON MOTOR EVOKED POTENTIALS IN NEUROSURGERY A PROSPECTIVE RANDOMISED SINGLE BLINDED **OBSERVATIONAL** STUDY" had been approved by IEC on 16th December 2017 (IEC/1152). I had applied for CTRI (clinical trial registry - India) with reference number REF/2018/04/019668.

CTRI has suggested changing the study type from observational to interventional. Therefore, I would be grateful if you could accept my request of changing my study proposal title to "COMPARISON OF EFFECTS OF PROPOFOL AND DEXMEDETOMIDINE ON MOTOR EVOKED POTENTIALS IN NEUROSURGERY A PROSPECTIVE RANDOMISED SINGLE BLINDED **INTERVENTIONAL** STUDY".

Principal Investigator: Dr Soniya Biswas, Senior Resident - Neuroanesthesiology, Department Of Anaesthesiology, SCTIMST, Degree: MBBS, MD (Anaesthesiology)

I am enclosing herewith the CTRI suggestions and my IEC approval letter.

Thanking you,

Yours sincerely

Soniya Biswas
Senior resident, Neuroanesthesia
Department of Anesthesiology,
SCTIMST

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee

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

SCT/IEC/1152/JUNE-2018

19.06.2018

Dr. Soniya Biswas
Resident
Department of Anaesthesiology
SCTIMST, Thiruvananthapuram

Dear Dr. Soniya Biswas,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "COMPARISION OF EFFECTS OF PROPOFOL AND DEXMEDETOMIDINE ON MOTOR EVOKED POTENTIALS IN NEUROSURGERY. A PROSPECTIVE RANDOMISED SINGLE BLINDED OBSERVATIONS STUDY" (IEC/1152)" on 16th June, 2018.

The following documents were reviewed:

1. *Covering letter addressed to the Member Secretary, IEC, SCTIMST*
2. *Copy of IEC Application Form*
3. *CTRI email*

The following members of the Ethics Committee were present at the meeting held on 16th June, 2018 at Noshir H Wadia Conference Hall, AMCHSS, SCTIMST

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. Rema M. N	MD	Female	Basic Medical Scientist	No
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
5.	Dr. S S Giri Sankar	LL.M. Ph.D.	Male	Legal Expert	No
6.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
7.	Mr. Satheesh Chandran	MSW, PGDPM	Male	Lay person/ NGO/ Social Scientist	No
8.	Dr. Harikrishna Varma PR	Ph.D(Materials Science)	Male	Medical Technology	Yes
9.	Dr. P. Manickam	BSMS, MSc (Epid).,PhD	Male	Health Science Expert/ Social Scientist	No
10.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
11.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
12.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
13.	Dr. Anand Kumar A	MD, DM	Male	Clinician	No
14.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
15.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The revised title is approved.

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/2017/683 **Date:17.11.2017**

Project title: COMPARISON OF EFFECTS OF PROPOFOL AND DEXMEDETOMIDINE ON MOTOR EVOKED POTENTIALS IN NEUROSURGERY A PROSPECTIVE RANDOMISED SINGLE BLINDED OBSERVATIONAL STUDY.

Principal Investigator:
Dr. Soniya Biswas Degree: MBBS, MD(Anaesthesiology) Resident, Department of Anaesthesiology, SCTIMST
Co-Principal Investigator(s)
Dr. Smita V. Degree: MBBS, MD(Anaesthesiology), DM(Neuroanaesthesiology) Associate Professor, Department of Anaesthesiology, SCTIMST
Dr. Unnikrishnan P. Degree: MBBS, MD (Anaesthesiology), PDCC(Neuroanaesthesiology) Assistant Professor, Department of Anaesthesiology, SCTIMST

Members who participated in the TAC meeting on 11/09/2017
Dr. Rupa Sreedhar (Chairperson)
Dr. Prasantakumar Dash
Dr. Sanjay G
Dr. Krishna Kumar K
Dr. Syam K
Dr. Bijulal S
Dr. Varghese T. Panicker
Dr. Jayadevan E.R.
Dr. K. Shivakumar (Member Secretary)

Dr. Jayadevan E.R, Dr. Bijulal S, Dr. Syam. K, Dr. Sanjay G, Dr. Krishna Kumar K, Dr. Rupa Sreedhar and Dr. Varghese T. Panicker stayed away from the proceedings when the projects in which they are involved as investigator were discussed (#676,677,680,685,687,690,693,694).

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.

Signature of the Member Secretary, TAC (Clinical Studies)

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

Plagiarism Checker X Originality Report

Plagiarism Quantity: 5% Duplicate

Date	Saturday, July 27, 2019
Words	711 Plagiarized Words / Total 14571 Words
Sources	More than 545 Sources Identified.
Remarks	Low Plagiarism Detected - Your Document needs Optional Improvement.

Intraoperative neurophysiological monitoring (IONM) is often used in various intracranial and spine procedures to prevent damage to eloquent areas, cranial nerves or motor or sensory tracts. Motor evoked potential (MEP) monitoring is invariably an essential tool in the armamentarium of the operating surgeons to avoid injury to the motor tract in various intracranial and spine surgeries.

(1) Transcranial motor evoked potential (TcMEP) monitoring is stimulation of the motor cortex through the skull and eliciting compound muscle action potentials (CMAP) from the peripheral muscles to test the intactness of the motor pyramidal pathway. (1) TcMEP is being used in surgeries for monitoring and mapping of the motor pathways. It is used in the mapping of the motor cortex in resection of tumour or arteriovenous malformation located near the motor cortex or in epilepsy surgeries. It is also used in the subcortical mapping of corticospinal tract. It is also used in brainstem surgeries and in Chiari malformation.

It is also used in vascular surgeries like carotid endarterectomy, reconstructive surgeries of the neck, aneurysms of the aortic arch and of thoracoabdominal aorta or intracerebral aneurysms of middle or anterior cerebral arteries. It is very commonly used in spinal surgeries for extradural or intradural (extramedullary or intramedullary) tumour resection, embolization of arteriovenous malformations and in deformity corrective surgeries like scoliosis and spondylolisthesis.

(2) Intraoperatively, there are many factors other than surgical manipulation that can affect the quality of the CMAP like temperature, blood pressure, partial pressure of expired carbon dioxide, oxygen, etc. These factors need to be optimized for correct interpretation of the MEPs. (2) The anaesthetic agents can affect the quality of MEP intraoperatively as they inhibit synaptic transmission. Muscle relaxants antagonize the transmission of signals across the neuromuscular junction.

Inhalational agents suppress the CMAP and should be used at a lower minimum alveolar concentration (MAC). Opioids seem to have very little effect on CMAP. Intravenous anaesthetics suppress MEP lesser than inhalational agents, so total intravenous anaesthesia(TIVA) or combination of intravenous with minimal

Sources found:

Click on the highlighted sentence to see sources.

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s no	age	sex	asa	diagnosis	weight	height	duration of anaesthesia	duration of sx	motor power rul	lul	rll	lll	current(mA)	rul T1 amplitude	rul T1 latency	rul T2 amplitude	rul T2 latency
1	32	f	1	cervical	80	162	240	300	4	4	4	4	100	41	21	45	21
2	18	m	1	thoracic	60	154	180	240	5	5	4	4	100	236	24	236	24
3	58	f	2	lumbar	56	150	180	240	5	5	5	5	99	300	24	312	24
4	51	f	2	cervical	60	156	180	240	4	5	5	5	121	138.8	21.3	138	21.5
5	46	f	2	cervical	70	161	240	300	4	4	5	5	135	687.8	25.3	700	25.8
6	64	m	2	cervical	64	163	180	240	5	5	5	5	112	91	37.7	98.4	37.2
7	20	f	1	cervical	46	150	180	240	4	4	5	5	130	234	20	235	20
8	42	m	2	lumbar	70	165	180	240	5	5	4	4	170	512	26	514	26
9	32	m	1	cervical	64	163	180	240	4	5	5	5	167	57.9	10	60	10
10	30	f	1	thoracic	64	167	180	240	5	5	5	5	150	145	28	145	28
11	60	m	2	cervical	46	160	180	240	4	4	5	5	150	214.7	30.8	209.7	31.7
12	45	f	2	lumbar	72	170	180	240	5	5	5	4	160	250	23	250	23
13	45	f	2	cervical	70	172	300	360	4	4	5	5	100	150	24.5	151	24.5
14	15	m	1	cervical	40	153	240	300	5	5	5	5	100	71	31	74.5	31
15	28	m	1	cervical	56	161	180	240	4	5	5	5	170	46.9	61.2	48	60.3
16	54	m	2	thoracic	64	159	240	300	5	5	5	5	120	200	34	201	34
17	42	f	2	lumbar	70	164	180	240	5	5	5	5	120	123	15	125	15
18	30	m	1	lumbar	65	164	180	240	5	5	5	5	130	234	23	234	23
19	34	f	1	cervical	88	168	240	280	5	5	5	5	133	47.9	22	44.8	23.5
20	45	m	2	cervical	60	162	240	300	4	4	4	4	108	23.7	36.5	22.6	36.7
21	48	f	2	thoracic	50	160	240	300	5	5	4	5	110	112	10	112	10
22	59	f	2	thoracic	60	156	180	240	5	5	5	5	124	219	24	220	24
23	47	m	2	cervical	72	163	180	240	4	5	5	5	113	140	22.3	141	22
24	60	f	2	cervical	60	157	300	350	4	4	5	4	140	154	28	155	28

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amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency
43	21	41	21	44	21	51	24	53	24	54	23	54	23	56	23		
234	24	236	24	234	24	257	25	257	25	254	25	254	25	256	25	33.6	25
300	24	301	24	302	24	311	21	312	21	316	21	316	22	316	21	242.8	31.8
138	21.8	138.9	21.6	138.8	21.7	131.5	25	130	25	130	25	130	25.2	130	26		
700	23.3	700	25.8	700	27	814	32	814	34.2	824	33.7	824	33	814.6	32.8		
92.6	37.2	91.7	37.8	91.3	37.8	100	27.2	96	27.1	97	26	97	26	97	26		
234	20	234	20	235	20	295	24.2	295	24.2	290	23.5	294.5	23.3	294	23.4		
511	26	512	26	512	26	453	25	453	25	455	25	453	26	453	25	300	37.5
61	10	60	10	60	11	112	25	115	25	100	26	113	26	115	26		
145	28	145	29	147	28	200	28	200	28	201	28	202	28	203	18	218	31.7
205.1	31.5	199.2	31	214	31.8	189	27	189	27	190	27	190	27	191	27		
253	23	251	23	253	23	200	25	201	25	201	21	202	21	203	21	137.8	26
154	24.5	154	24.5	154	24.5	120.7	30.2	120.8	30.2	121.2	29.8	121.3	30	120	30		
74	31	74	31	74	31	250	24.8	250	24.8	258	22.5	252.2	22.4	252	22.4		
48	56.3	48	57.5	48	57.4	122	38.3	122	38.5	121	38.8	120	38.8	121	38.8		
201	34	201	34	201	34	178	30	178	30	177.5	30	178	30	178	30	255.7	33
125	15	125	15	125	15	148	20	145	20	145	21	147	22	148	20	240	35.2
235	23	236	23	238	23	235	27	231	27	231	27	231	27	231	27	100	35
55.9	24	50.6	23.3	55	23.3	69	25	68	25	68	25	68	25	69	25		
15	36.8	25.4	36.2	14.8	36.5	50	24	46	25	48	24	47	24	47	24		
114	9	115	10	115	10	45	25	48	25	48	25	45	25	45	25	138	24.8
221	24	220	24	219	24	169	33	170	33	170	33	170	33	170	33	136	22.5
141	22.5	141	22.6	141	22.6	71	32.1	72	31.8	72	31.9	70	31.8	70	31.8		
154	28	154	28	154	28	51	30	51	30	50	30	50	30	50	30		

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t2		t3		t4		te		III t1		t2		t3		t4		te	
amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amp	lat	amp	lat	amp	lat
34	25	33.6	25	33.6	26	33	26	33.6	25	34	26	34	25	33.6	25	33	25
242.8	31.8	243	31.8	242.8	32	242	32	242.8	31.8	242.8	31.8	243	32.9	242.8	31.8	242	31.8
300	37.5	300	37.5	300	37.5	300	37.5	300	37.5	300	37.5	300	37.5	300	37.5	300	37.5
218	31.7	218	31.7	218	31.7	218	31.7	210	31.7	218	31.7	218	31.7	218	32	218	31.7
137.8	25.7	137.8	25.7	138	25.7	137.8	25.7	137.8	25.7	137.8	25.7	137.8	25.7	138	25.7	137.8	25
255.7	33	255.7	33	255.7	33	255.7	33	255.7	33	256	33	255.7	33	255	33	255.7	33
240	35.2	240	35.2	240	35.2	240	35.2	240	35.2	240	35.2	240	35.2	240	35.2	240	35
100	35	100	33	100	33	100	33	100	33	100	33	100	33	100	33	100	33
138	25	138	25	139	25	138	25	138	25	138	25	138	25	139	26	138	25
136	22.4	136	23	136	23	136	24	136	23	134	23	135	23	138	23	136	23

PROPOFOL

fentanyl bolus frequency	hemo+psi +drugs during stimulation																	
	t1							t2							t3			
	hr	bp	map	psi	propofol	fentanyl	fentanyl bo	hr	bp	map	psi	propofol	fentanyl	fentanyl bo	hr	bp	map	
0	72	93/66	70	29	468	201	0	72	93/66	70	29	568	214	0	72	93/66	70	
0	105	93/57	60	24	220	190	0	105	93/57	60	24	330	200	0	105	93/57	60	
0	72	93/66	69	28	230	199	0	72	93/66	69	28	280	208	0	72	93/66	69	
0	74	105/62	70	28	340	170	0	74	105/62	70	28	410	180	0	74	105/62	70	
0	57	97/50	69	28	350	210	0	57	97/50	69	28	400	221	0	57	97/50	69	
1	62	120/60	87	27	360	324	0	62	120/60	87	27	430	334	0	62	120/60	87	
1	62	115/60	78	27	180	454	0	62	115/60	78	27	210	461	0	62	115/60	78	
0	88	102/60	71	30	320	210	0	88	102/60	71	30	360	221	0	88	102/60	71	
0	70	92/46	61	30	270	180	0	70	92/46	61	30	310	190	0	70	92/46	61	
1	70	92/58	69	29	327	418	0	70	92/58	69	29	400	428	0	70	92/58	69	
1	65	121/80	89	30	270	228	0	65	121/80	89	30	330	236	0	65	121/80	89	
1	84	111/58	76	29	390	303	0	84	111/58	76	29	470	314	0	84	111/58	76	
1	54	118/68	75	27	300	309	0	54	118/68	75	27	360	320	0	54	118/68	75	
0	64	109/60	76	28	194	210	0	64	109/60	76	28	224	216	0	64	109/60	76	
1	60	108/60	73	27	321	340	0	60	108/60	73	27	360	350	0	60	108/60	73	
0	64	107/68	72	30	290	182	0	64	107/68	72	30	330	192	0	64	107/68	72	
1	60	109/64	71	29	320	281	0	60	109/64	71	29	380	292	0	60	109/64	71	
0	74	121/80	84	30	270	230	0	74	121/80	84	30	320	240	0	74	121/80	84	
0	80	114/65	76	35	420	198	0	80	114/65	76	35	510	212	0	80	114/65	76	
1	60	98/62	68	31	319	296	0	60	98/62	68	31	384	306	0	60	98/62	68	
0	79	111/70	73	35	207	232	0	79	111/70	73	35	242	238	0	79	111/70	73	
1	47	112/52	72	35	343	502	0	47	112/52	72	35	416	512	0	47	112/52	72	
1	66	103/66	70	35	372	366	0	66	103/66	70	35	447	376	0	66	103/66	70	
1	69	128/70	89	36	279	416	0	69	128/70	89	36	332	426	0	69	128/70	89	

PROPOFOL

				t4							hemo+drug+psi preop					after induction	
psi	propofol	fentanyl	fentanyl bo	hr	bp	map	psi	propofol	fentanyl	fentanyl bo	hr	bp	map	psi	hr	bp	map
29	668	227	0	72	93/66	70	29	768	240	0	70	117/74	88	90	74	85/53	59
24	380	210	0	105	93/57	60	24	428	220	0	100	123/72	92	100	113	88/45	58
28	330	217	0	72	93/66	69	28	380	226	0	70	117/74	86	100	74	85/53	57
28	480	190	0	74	105/62	70	28	540	200	1	89	135/75	102	98	89	94/50	60
28	450	232	0	57	97/50	69	28	500	243	0	61	100/60	69	95	65	84/50	61
27	513	344	0	62	120/60	87	27	593	354	1	60	140/80	100	98	60	60/30	49
27	240	468	0	62	115/60	78	27	276	475	1	62	105/52	71	90	63	103/50	70
30	400	232	0	88	102/60	71	30	444	242	0	80	140/90	105	84	84	100/70	69
30	350	200	0	70	92/46	61	30	391	210	0	72	110/80	79	90	72	110/72	72
29	470	438	0	70	92/58	69	29	533	448	0	93	127/78	83	91	87	106/61	71
30	390	244	0	65	121/80	89	30	450	252	1	80	120/80	83	95	65	105/70	71
29	550	325	0	84	111/58	76	29	635	336	0	64	126/64	87	96	60	126/82	85
27	425	331	0	54	118/68	75	27	485	342	1	70	110/59	70	91	62	95/59	68
28	254	223	0	64	109/60	76	28	284	230	0	70	110/70	74	90	65	100/60	68
27	303	360	0	60	108/60	73	27	343	370	0	68	121/70	79	94	60	108/60	71
30	386	202	0	64	107/68	72	30	426	212	0	80	121/80	79	99	65	103/60	70
29	440	303	0	60	109/64	71	29	506	314	1	70	112/50	70	98	60	99/50	68
30	370	250	0	74	121/80	84	30	427	260	1	116	118/90	72	90	80	100/60	69
35	600	226	0	80	114/65	76	35	686	240	1	124	120/80	80	95	90	100/60	70
31	449	316	0	60	98/62	68	31	514	326	0	88	106/67	70	98	70	100/70	69
35	277	244	0	79	111/70	73	35	312	250	0	84	115/63	73	98	75	103/55	70
35	489	522	0	47	112/52	72	35	562	532	0	64	154/77	108	99	48	117/54	73
35	522	386	0	66	103/66	70	35	597	396	0	101	113/65	72	98	85	99/70	68
36	385	436	0	69	128/70	89	36	438	446	1	70	130/70	90	98	60	112/65	71

PROPOFOL

after intubation				5 min				10 min				15 min				30 min
psi	hr	bp	map	psi	hr	bp	map	psi	hr	bp	map	psi	hr	bp	map	psi	hr
35	76	186/85	118	35	76	100/59	60	34	74	76/55	50	30	73	89/30	54	30	72
23	120	116/69	75	24	108	103/73	69	25	101	97/69	60	24	105	83/56	59	23	105
30	76	186/85	120	32	76	100/59	69	30	74	76/55	54	30	73	89/30	60	30	72
26	84	138/87	98	27	95	112/60	72	28	84	120/80	80	29	81	115/80	73	30	74
30	80	110/60	72	31	70	109/60	70	28	65	93/54	69	28	63	95/54	68	28	57
28	62	95/50	69	28	62	95/50	68	27	63	86/42	63	28	62	95/52	68	28	62
26	63	120/70	80	30	64	117/63	75	27	64	116/70	71	27	64	114/61	72	27	62
31	90	140/90	90	31	80	101/67	69	30	82	101/60	69	30	85	100/60	70	30	88
31	90	112/72	76	30	80	110/70	71	30	71	91/47	66	30	67	90/40	67	30	70
30	75	150/94	97	30	75	149/86	98	30	72	121/68	81	30	66	96/57	66	30	70
26	75	130/80	91	30	71	120/82	80	30	65	119/78	79	30	65	120/80	80	30	65
31	64	130/70	92	30	69	112/49	73	30	57	91/41	69	30	59	101/40	68	29	84
28	69	114/64	76	30	63	103/62	70	30	60	100/61	70	30	60	84/49	63	28	54
29	72	111/70	74	28	65	109/70	75	28	65	108/60	71	28	64	108/60	70	28	64
27	70	120/80	80	27	60	105/65	72	27	60	108/60	71	27	60	108/60	70	27	60
32	65	125/80	83	31	65	110/70	76	33	66	109/70	71	32	65	109/68	70	31	64
29	70	120/80	80	30	65	102/60	70	30	64	105/60	70	30	63	107/60	70	30	60
27	97	130/80	89	28	82	120/80	80	29	74	120/80	86	30	75	120/81	84	30	74
33	110	120/85	85	34	86	116/70	75	34	84	115/70	73	35	80	115/70	73	35	80
32	80	122/81	86	31	74	112/72	75	32	59	100/69	69	32	59	100/70	68	32	60
36	90	125/80	87	36	85	120/80	83	35	81	117/70	74	35	78	116/64	75	32	79
35	55	119/60	79	35	51	103/49	69	35	49	99/51	70	36	48	109/54	70	35	47
35	86	112/62	75	36	86	98/57	65	35	86	102/64	69	35	67	108/48	69	35	66
37	68	126/61	89	35	65	130/70	92	35	68	128/70	89	36	68	127/70	90	37	69

PROPOFOL

			45 min				1 hr							1.5 hr				2 hr
bp	map	psi	hr	bp	map	psi	hr	bp	map	propofol	fentanyl	psi	hr	bp	map	psi	hr	
97/66	70	30	73	93/66	70	30	70	111/78	70	768	240	29	70	110/78	70	28	70	
82/49	60	23	110	93/57	68	23	113	88/56	60	428	220	24	127	99/52	68	22	106	
97/66	69	30	73	93/66	69	28	70	111/78	69	380	226	28	69	109/80	70	28	66	
103/50	70	30	73	105/62	70	30	78	99/53	68	540	200	28	90	115/67	74	30	89	
93/54	69	28	60	97/50	70	28	66	110/64	70	485	230	28	70	110/64	74	28	72	
108/50	87	28	70	120/60	87	27	70	120/60	79	593	354	27	70	108/57	70	27	70	
114/60	78	28	60	115/60	78	27	61	118/60	75	276	475	27	60	120/80	71	27	65	
90/60	71	30	80	102/60	71	30	80	105/60	69	444	242	30	80	110/70	81	30	80	
90/45	61	30	70	92/46	68	30	70	104/46	70	391	210	30	70	110/70	74	30	70	
105/59	69	30	68	92/58	69	29	64	99/64	68	533	448	29	63	107/65	80	29	62	
120/80	89	30	67	121/80	89	30	68	120/80	73	450	252	30	70	120/80	79	30	65	
124/61	76	29	75	111/58	76	30	67	107/51	70	635	336	29	61	102/60	71	30	59	
110/61	75	28	52	118/68	75	28	52	118/68	75	485	342	27	56	118/66	74	27	56	
109/60	76	28	65	109/60	76	28	65	110/60	70	284	230	28	65	110/60	70	27	64	
107/60	73	27	60	108/60	73	27	60	107/62	69	343	370	27	60	105/60	70	27	60	
109/68	72	32	65	107/68	72	32	60	108/65	71	426	212	30	60	109/65	70	30	62	
108/60	71	30	60	109/64	71	30	63	108/60	70	506	314	29	60	107/63	70	29	60	
124/80	84	30	75	121/80	84	30	76	120/80	78	427	260	30	75	121/80	76	30	74	
116/70	76	35	78	114/65	76	34	78	115/65	73	686	240	35	80	118/68	72	35	78	
99/69	68	32	59	98/62	68	32	59	97/62	68	514	326	31	65	102/65	72	31	62	
115/64	73	33	75	111/70	73	34	76	110/70	70	312	250	35	78	110/71	74	35	76	
121/70	72	35	47	112/52	72	35	49	112/58	71	562	532	35	48	120/60	81	35	49	
107/32	70	35	67	103/66	70	35	78	123/57	83	597	396	35	68	115/69	74	35	68	
126/70	89	36	68	128/70	89	36	69	125/60	84	438	446	36	65	122/78	78	37	62	

PROPOFOL

bp	map	propofol	fentanyl	psi	2.5 hr	bp	map	psi	3 hr	bp	map	propofol	fentanyl	psi	3.5 hr	bp	map
109/78	70	1376	310	27	70	108/78	70	27	70	110/78	70	1984	390	27	70	110/64	70
108/73	68	736	340	23	102	104/63	68	24	101	103/64	68	1044	400	25			
108/73	70	648	288	28	66	108/64	70	28	68	109/65	70	916	350	28			
115/70	74	960	260	30	90	115/69	74	29	90	112/64	74	1380	320	29			
107/63	74	830	300	28	70	104/63	74	28	70	117/72	74	1175	370	28	65	108/62	70
101/60	70	1058	430	27	70	105/60	70	28	70	109/60	70	1523	480	28			
116/78	71	460	535	27	69	114/60	71	28	69	112/65	71	644	594	27			
115/70	81	748	314	30	80	120/80	81	30	78	122/80	81	1052	384	30			
109/68	74	654	270	30	70	108/60	74	30	71	110/70	74	917	340	30			
112/63	80	938	515	28	65	120/80	80	28	70	120/80	80	1343	575	28			
122/80	79	808	510	31	66	120/78	79	31	65	120/77	79	1166	560	31			
111/58	71	1126	378	29	60	112/60	71	29	61	113/60	71	1617	440	29			
119/68	74	830	408	28	55	113/64	70	27	54	110/60	70	1175	480	27	56	112/60	72
110/60	70	488	290	28	65	110/60	70	28	65	110/62	70	692	340	28	65	110/64	71
108/60	70	574	430	27	60	108/60	70	27	60	109/62	70	777	486	27			
109/68	70	724	272	28	63	109/70	70	30	60	109/60	70	1022	332	30	60	110/67	71
109/60	70	872	390	29	60	110/60	70	29	60	109/58	70	1238	450	29			
120/75	76	724	330	30	75	120/70	76	29	76	118/70	76	1021	400	29			
119/64	72	1196	350	35	75	116/64	72	35	72	112/64	72	1706	440	35	70	110/70	71
100/70	72	908	480	31	63	107/69	72	31	63	108/60	72	1302	540	31	63	108/60	73
110/70	74	524	300	35	75	110/70	74	35	72	111/70	74	736	360	35	70	112/70	72
130/70	81	1004	890	35	50	128/70	81	35	50	129/71	81	1446	950	35			
115/68	74	1050	464	35	68	113/59	74	35	68	114/58	74	1503	534	35			
120/75	78	756	520	36	62	120/72	78	36	63	119/79	78	1074	580	36	65	125/70	75

PROPOFOL

psi	4 hr hr	bp	map	propofol	fentanyl	psi	4.5 hr hr	bp	map	psi	5 hr hr	bp	map	propofol	fentanyl	psi	propofol infusion rate
	27	70 110/65	70	2592	470	27											7.6
																	5.14
																	4.79
																	7.1
	28	60 104/62	69	1520	440	28											4.94
																	7.28
																	4
																	4.35
																	4.11
																	6.33
																	7.8
																	6.83
	27	57 110/62	71	1520	640	27	57 112/64	71	27	57 110/64	70	1865	700	27	4.94
	27	66 110/60	71	896	380	28											5.12
																	4.13
	30	63 110/60	71	1320	392	30											4.67
																	5.23
																	4.57
	35	70 111/70	71	2216	530	35											5.8
	31	63 112/71	71	1696	600	31											6.57
	35	72 112/70	70	948	420	35											4.25
																	7.37
																	6.3
	35	60 118/78	74	1392	650	35	60 120/70	74	35	60 117/74	72	1710	720	35	5.3

PROPOFOL

Recovery after stopping the anaesthetic drugs						complications								
respiration	spont	movi	extubation	verbal	orientation	icu	dischar	bradycardi	tachycardia	hypotensio	hypertensi	respiratory	movement	any injury	new deficit	intraop awareness
25	40	48	52	65	800	0	0	0	0	0	0	0	0	0	0	0
10	15	20	20	60	720	0	0	1	0	0	0	0	0	0	0	0
12	18	22	25	60	480	0	0	1	0	0	0	0	0	0	0	0
8	12	15	16	30	500	0	0	0	0	0	0	0	0	0	0	0
15	20	30	35	45	700	1	0	1	0	0	0	0	0	0	0	0
10	17	23	28	34	800	0	0	1	0	0	0	0	0	0	0	0
12	15	20	25	30	500	0	0	0	1	0	0	0	0	0	0	0
10	14	18	22	29	800	0	0	0	0	0	0	0	0	0	0	0
10	15	20	24	30	700	0	0	1	0	0	0	0	0	0	0	0
20	30	37	39	45	800	0	0	0	1	0	0	0	0	0	0	0
10	15	17	19	30	800	0	0	0	1	0	0	0	0	0	0	0
10	14	18	20	25	800	1	0	1	1	0	0	0	0	0	0	0
20	28	34	40	50	950	1	0	0	1	0	0	0	0	0	0	0
25	30	35	37	45	2500	0	0	0	0	0	0	0	0	0	0	0
15	20	25	28	34	900	0	0	0	0	0	0	0	0	0	0	0
15	25	29	31	35	800	0	0	0	0	0	0	0	0	0	0	0
10	15	17	18	25	500	0	0	0	0	0	0	0	0	0	0	0
20	23	24	26	30	600	0	0	0	0	0	0	0	0	0	0	0
20	23	26	27	31	780	0	0	0	0	0	0	0	0	0	0	0
20	28	35	37	42	840	1	0	0	1	0	0	0	0	0	0	0
25	28	32	35	40	900	0	0	0	1	0	0	0	0	0	0	0
15	19	26	32	40	900	1	0	1	1	0	0	0	0	0	0	0
20	24	29	34	44	750	0	0	0	0	0	0	0	0	0	0	0
15	20	23	27	30	900	0	0	0	1	0	0	0	0	0	0	0

Dexmedetomidine- Group D

s no	age	sex	asa	diagnosis	weight	height	duration of sx	duration of anaesthesia	motor power rul	lul	rll	lll	current	rul t1		t2		t3
														amplitude	latency	amplitude	latency	amplitude
1	49	m	2	thoracic	80	168	300	360	5	5	5	5	110	130	25	124	27	130
2	55	f	2	thoracic	60	156	300	360	5	5	4	4	150	312	28	270	31	310
3	50	f	2	cervical	56	158	180	240	4	4	5	5	150	63.8	22	61	24.8	62.8
4	43	f	2	lumbar	60	161	240	300	5	5	5	4	156	200	28	150	31	199
5	28	f	1	thoracic	70	163	240	300	5	5	5	5	100	300	40	270	43	299
6	59	m	2	lumbar	64	160	180	240	5	5	5	5	159	158	22	123	27	158
7	18	f	1	lumbar	46	154	120	180	5	5	5	5	159	198	25	140	29.8	197
8	58	f	2	cervical	70	160	180	240	4	4	5	5	150	140	23.8	125	24	139
9	47	m	2	cervical	64	159	120	180	4	4	5	5	150	172.8	27.1	164	27.5	171
10	49	f	2	lumbar	64	160	300	360	5	5	4	5	160	234	33	212	36	231
11	31	f	1	cervical	46	152	120	180	4	5	5	5	110	118.1	27	110	28	112
12	34	m	1	cervical	72	171	120	180	4	5	5	5	150	72.5	24	72.5	26.2	75.5
13	53	f	2	lumbar	70	168	120	180	5	5	5	5	142	200	25	178	27	198
14	27	m	1	cervical	40	156	120	170	4	4	5	5	142	29.7	26	21.4	27	29
15	37	f	2	cervical	56	156	120	180	4	4	5	5	150	138	30	130	33	137
16	34	m	1	cervical	64	162	120	180	4	5	5	5	100	212	24.3	189	25.4	210
17	56	m	2	cervical	70	169	180	235	4	4	5	5	134	172	35.6	168	35.8	169
18	24	f	1	cervical	65	167	240	300	4	4	5	5	151	150	21	147	22.5	149
19	34	m	1	cervical	88	170	120	180	5	5	5	5	90	304	29	270	31.2	298
20	21	m	1	lumbar	60	162	240	300	5	5	4	5	100	350	25	300	28	345
21	50	f	2	lumbar	50	156	120	178	5	5	4	5	160	248	27	220	31	250
22	22	m	1	lumbar	60	157	180	230	5	5	5	4	143	169	23	140	25	168
23	48	f	2	lumbar	72	162	120	180	5	5	5	5	150	200	24.5	170	27	190
24	38	m	1	cervical	60	160	180	240	4	4	5	5	100	213.4	24	198.7	26.7	213.7

Dexmedetomidine- Group D

					lul										rll			
t4		te		t1		t2		t3		t4		te		t1		t2		
latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	
26	131	25	131.7	25	131	28	125	31	129.5	30	131	28	131	28	158	30.2	120	
28.6	310	28	312	28	300	27	240	30	292	27	300	26	300	26	157	25	130	
23	63.5	22.7	63.5	22	13.9	20	52.6	22.8	93	21.5	93.1	20	93.9	20				
29.5	200	29	200	28	190	29	145	32	192	30	200	30	200	30	115	33.8	108	
40.8	300	40	300	40	320	38	290	41	321	39.7	322	39	320	39	157.2	25	137	
23	158	22.7	158	22	170	34	165	35	170	34.3	173	34	174	34	156	39.2	155	
26	197	25	198	25	200	22	160	24	209	23	210	23	213	22	117	43	112	
23.9	140	23	140	23	130	29	93	31	108	30	110	29	110	29				
27.3	171	27.2	171	27.2	150	26	130	28	131	27	131.2	26	132	26				
34.5	234	33	234	33	200	27	165	29	200	28	201	27	200	27	315	30.3	310	
28	117	28	117	28	140.9	27	135	27.1	136	27	138	27	138	27				
26	76.5	25	76.5	25	167.9	31	160	33	168	33	168.9	33	169	33				
26	200	25	200	25	150	27	120	29	148	27.4	150	27	151	27	163	15.2	135	
26.8	29	26	29.7	26	49.7	25	35	26	39	25	40	25	41	25				
31.8	136	30	137	30	118.5	26	113	27.2	113	27	113	26.5	111	26				
25.3	210	25.4	212	25.3	188.8	21	136.5	24.5	136.5	22	137.5	21	137	21				
35.7	169	35.7	170	35.2	118	29	115	30.3	118	29	118	28	118	28				
21.5	149	21.4	149.5	21	187	25	187	27.6	187	27	187	26	188	26				
31	300	31.1	302	31	403.4	21	378	22.8	378	22	378	22	377	22				
27	350	25	350	25	298	24	260	26.8	299	25.7	299	25	300	25	298	35.2	280	
30	249	27	249	27	300	29	250	32	309	30	310	29	310	29	173	27	170	
23.5	169	23	170	23	156	24	134	26.8	158	24.4	160	24	160	24	199	32.3	180	
26.7	190	24.6	200	24.6	200	25	170	26.5	209	25.5	210	25	210	25	140	35	120	
26	213.7	24	213.1	24	200	28	187	28	198	27	199	27	200	27				

Dexmedetomidine- Group D

t3		t4		te		lll t1		t2		t3		t4		te			
latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	amplitude	latency	fentanyl	bo
32.2	141	31	157	30	157	30	158	30.2	120	32.2	150	31	157	30	157	30	1	
25.2	150	30.2	157	27.3	157	26	157	25	130	25.2	150	30.2	157	27.3	157	26	1	
																	1	
35	110	35	115	34	117	34	115	33.8	108	35	110	35	115	34	117	34	0	
32.2	150	28.5	157	29.5	157	23.2	157.2	20	140	25	150	24	157	20	157	20	1	
39.8	150	40.3	157	39.3	157	36.2	156	39.2	147	39.8	150	40.3	157	39.3	157	36.2	1	
43.2	117	43.2	117	43.2	117	43.3	117	43	112	43.2	117	43.2	117	43.2	117	43.3	0	
																	0	
																	1	
32	310	31	315	31	317	30.3	315	30	308	32	310	31	315	30.1	317	30.3	1	
																	0	
																	1	
18	160	17.8	163	17.5	163	17.3	167	18	135	20	157	20	163	18	163	20	1	
																	0	
																	0	
																	0	
																	1	
																	0	
																	1	
35.3	285	35.3	298	35.3	299	35.4	295	35.2	280	35.3	289	35.3	298	35.3	299	35.4	1	
27.7	173	27.8	173	27.7	170	27	173	27	169	27.7	173	27.8	173	27	170	27	0	
32.5	187	32.5	199	32.5	198	32.5	200	32.3	180	32.5	187	32.5	199	32.5	198	32.5	0	
35.2	140	35.2	143	35.2	143	35.2	140	35	120	35.2	135	35.2	143	35	143	35.2	0	
																	0	

Dexmedetomidine- Group D

+drugs during stimulation	t1						t2							t3		
hr	bp	map	psi	propofol	fentanyl	fentanyl bo	hr	bp	map	psi	propofol	fentanyl	fentanyl bodexim	hr	bp	map
70	120/80	80	35	450	300	1	55	140/70	112	33	660	412	1 40	51	140/68	100
50	105/60	69	30	350	240	0	46	100/70	70	28	500	250	0 30	46	95/50	69
69	100/58	65	35	350	224	0	68	98/56	69	35	400	236	0 28	69	100/57	70
78	105/70	69	35	340	200	0	56	98/54	67	33	400	209	0 30	56	98/55	68
80	112/70	71	30	300	436	0	60	130/80	94	31	312.5	442	0 35	56	132/80	95
70	120/80	80	30	240	336	0	55	107/65	72	29	300	348	0 32	55	108/65	71
76	103/65	69	30	340	218	0	66	100/60	69	29	360	224	0 23	65	100/62	70
60	105/60	69	30	580	269	0	50	145/67	123	28	600	278	0 35	50	120/70	80
70	124/75	80	28	370	430	1	50	140/90	118	26	400	436	0 32	50	138/78	99
56	103/63	69	30	500	375	0	51	126/74	87	26	600	386	0 32	57	108/60	74
75	112/70	71	29	560	220	0	51	100/68	70	28	600	230	0 23	52	106/68	72
65	120/73	80	30	460	430	0	56	127/74	88	28	500	442	0 36	52	120/62	81
72	121/80	80	32	450	300	1	55	145/95	116	28	650	511	0 35	53	140/70	102
70	112/70	72	29	182	213	0	54	100/70	69	27	200	217	0 20	53	101/70	69
75	115/70	72	29	270	330	1	60	102/68	71	29	300	340	0 28	59	104/68	70
68	102/70	69	35	350	224	0	54	140/70	109	27	400	230	0 32	54	141/70	109
75	120/80	80	30	620	312	1	52	140/95	115	30	650	324	0 35	52	140/90	116
64	111/75	72	29	550	311	0	53	100/71	70	29	600	322	0 32.5	51	99/64	69
70	108/70	70	29	400	242	0	55	130/80	96	28	450	357	0 44	54	125/78	84
65	112/75	71	29	450	220.2	0	52	140/95	118	29	500	330.2	0 30	53	135/78	96
70	120/70	76	31	460	226	0	52	130/70	96	29	490	235	0 25	53	124/70	85
68	112/70	70	29	500	260	0	54	106/70	72	27	530	270	0 30	52	102/70	70
65	115/70	72	30	450	230	0	53	100/63	70	30	500	242	0 36	52	102/60	68
60	109/70	70	29	400	310	0	49	135/80	97	29	450	320	0 30	50	130/82	93

Dexmedetomidine- Group D

												hemo+psi +drugs						
				t4								preop				after induction		
psi	dexim	fentanyl	fentanyl	bo	hr	bp	map	psi	dexim	fentanyl	fentanyl	bo	hr	bp	map	psi	hr	bp	map
34	46	424	0		50	135/70	97	34	52	436	0		70	140/90	106	98	83	133/80	94
28	35	260	0		48	95/50	67	28	40	270	0		60	144/84	108	89	54	116/69	78
34	32	242	0		68	100/58	70	34	40	254	0		93	116/78	78	91	85	93/56	70
30	35	228	0		57	100/56	70	29	35	237	0		76	107/68	70	90	78	87/48	67
29	41	448	0		56	128/86	85	29	47	454	0		65	115/60	78	91	70	94/50	69
30	37	360	0		56	109/65	74	29	42	372	0		83	125/74	86	95	61	119/72	73
28	27	230	0		65	100/64	70	30	31	236	0		76	100/70	69	98	69	100/57	70
28	41	287	0		50	115/65	76	28	47	296	0		82	146/92	121	95	56	83/64	60
26	37	442	0		50	135/75	97	26	42	448	0		80	125/67	89	98	70	110/60	71
26	37	397	0		55	108/60	75	26	42	408	0		72	107/58	73	99	66	89/49	59
27	29	240	0		52	105/67	73	27	35	250	0		90	117/78	76	95	78	100/65	70
28	48	460	0		51	124/66	85	28	56	472	0		93	129/66	87	96	86	106/55	71
28	41	570	0		52	130/65	94	28	47	576	0		80	130/80	94	95	70	112/70	73
27	23	221	0		52	101/70	70	27	26	226	0		70	116/77	76	94	62	105/60	70
28	33	350	0		58	102/70	70	28	38	360	0		86	120/74	80	96	65	102/60	69
27	37	236	0		54	135/70	94	28	41	242	0		80	130/70	90	99	70	99/50	66
29	40.8	336	0		52	140/85	102	29	46.6	348	0		80	130/80	93	93	68	112/70	72
29	37.9	333	0		51	101/70	70	29	43.3	344	0		75	116/75	75	94	60	108/65	71
28	51	372	0		54	121/72	83	28	58	387	0		76	124/80	86	95	65	100/70	70
28	36.4	440.2	0		52	130/70	95	28	42.8	450.2	0		69	135/70	95	96	60	112/65	71
29	31	241	0		53	123/70	86	29	37	246	0		78	120/80	82	96	68	103/65	71
27	35	280	0		51	104/68	72	27	40	290	0		65	120/80	83	97	59	100/70	70
29	48	254	0		51	103/60	73	29	60	266	0		82	124/75	86	95	60	109/70	73
29	35	330	0		50	128/80	86	29	40	340	0		69	120/70	80	95	59	106/63	72

Dexmedetomidine- Group D

after intubation				5 min				10 min				15 min				30 min	
psi	hr	bp	map	psi	hr	bp	map	psi	hr	bp	map	psi	hr	bp	map	psi	hr
35	92	144/99	117	34	86	98/57	67	34	85	105/61	71	34	77	125/70	85	34	77
34	63	143/68	116	35	52	97/49	66	32	57	100/54	67	32	54	98/55	67	32	50
35	94	107/62	73	35	88	109/65	75	34	80	105/63	71	35	82	105/65	70	35	89
40	78	109/75	74	40	70	103/68	70	34	67	101/63	69	35	66	105/66	70	35	63
30	78	103/70	71	31	70	104/70	69	30	75	105/70	70	30	72	106/68	70	30	70
30	75	135/85	99	31	70	120/85	85	30	70	120/85	85	30	67	108/70	72	32	67
32	83	117/79	78	31	83	104/64	70	30	80	100/62	69	30	78	87/61	59	30	76
28	58	149/76	123	29	60	136/81	93	30	60	116/64	73	29	59	108/69	70	29	59
28	80	140/80	116	28	70	133/82	95	28	65	128/80	85	28	64	128/76	84	28	60
30	67	98/62	70	29	64	95/52	69	28	61	92/46	62	28	61	99/55	69	28	50
29	86	130/80	98	30	80	120/78	84	29	78	116/76	78	29	70	111/70	74	29	68
30	86	130/58	99	31	80	120/73	83	30	87	113/67	73	29	77	103/56	70	29	77
29	85	131/80	96	30	80	125/70	83	29	78	118/70	78	28	75	119/70	80	29	72
28	68	118/78	76	29	61	112/70	72	29	60	110/70	74	29	61	109/70	71	29	60
30	75	125/78	85	30	72	118/70	75	29	70	115/70	76	29	68	112/68	73	29	65
30	80	110/70	72	30	75	107/60	71	30	70	105/60	70	29	68	107/60	70	29	69
29	80	127/78	86	30	75	121/70	83	30	70	116/67	78	30	68	115/67	73	30	65
29	70	116/71	75	29	64	111/71	76	29	63	110/70	74	29	62	110/70	74	29	62
28	78	114/74	74	30	72	110/70	74	29	70	108/70	71	29	68	107/69	71	29	68
29	78	130/80	98	30	72	125/65	83	30	68	120/80	89	29	65	115/65	76	29	65
31	80	122/84	89	31	74	119/70	76	31	72	116/65	75	30	68	114/62	73	30	68
29	68	121/84	84	30	65	118/74	74	29	65	115/74	74	29	64	111/70	74	29	63
31	70	130/80	96	31	66	121/74	85	30	65	119/70	78	30	64	115/67	75	30	60
29	64	110/70	71	29	60	108/71	76	29	60	109/70	72	29	60	108/69	71	29	60

Dexmedetomidine- Group D

45 min				1 hr				1.5 hr										
bp	map	psi	hr	bp	map	psi	hr	bp	map	psi	propofol	dexim	fentanyl	hr	bp	map	psi	
90/46	60	34	68	99/60	70	34	74	131/79	86	32	660	40	548	63	114/69	69	28	
90/54	60	31	50	103/56	71	30	50	93/46	68	28	500	31.2	260	60	125/60	71	28	
97/56	67	30	70	89/52	67	34	70	102/59	70	34	400	32	242	67	102/60	69	34	
101/60	69	35	56	98/64	69	30	55	92/63	67	28	400	35	237	50	93/59	67	28	
107/65	70	29	68	106/68	71	30	54	130/80	90	29	312	35	436	54	120/70	72	29	
110/70	74	29	68	112/70	75	30	68	113/70	74	30	300	0	336	58	109/65	70	30	
104/55	71	30	66	101/60	71	30	69	97/59	69	30	360	23	224	66	109/63	69	29	
103/50	71	29	60	102/59	70	29	50	145/67	108	27	600	35	278	50	129/73	89	28	
128/75	93	28	60	124/75	83	28	53	140/90	107	26	400	32	436	52	138/80	94	28	
103/63	70	27	53	97/62	69	26	50	120/74	83	26	500	32	380	57	111/70	87	28	
108/70	73	29	65	108/70	72	29	51	99/54	69	27	600	27	230	52	108/70	69	28	
107/56	73	29	75	108/57	72	29	52	124/64	84	28	500	24	454	52	123/62	84	28	
115/68	79	29	55	140/92	104	28	54	140/80	95	28	650	35	511	52	125/70	85	28	
108/70	71	29	53	99/64	69	27	53	102/64	68	27	200	40	221	52	104/68	68	28	
114/67	74	29	59	102/65	70	28	58	107/62	70	28	300	28	330	57	108/70	69	28	
110/62	73	29	53	140/70	104	28	52	137/68	87	28	400	32	224	53	135/68	82	28	
112/67	72	30	52	145/97	110	30	52	140/89	97	29	650	40.8	336	52	135/70	90	28	
109/70	70	29	51	100/62	65	29	51	99/61	68	27	600	38	333	52	105/64	67	28	
108/69	72	29	55	130/70	93	28	53	128/71	85	28	450	59	387	52	125/70	82	28	
112/75	74	29	53	145/94	112	29	52	140/80	103	28	500	36.4	410	52	135/75	84	28	
113/62	73	30	51	136/78	101	28	50	130/70	95	29	490	31	241	53	127/60	81	28	
110/70	74	29	62	111/65	72	29	60	112/70	75	29	530	0	260	51	108/70	70	28	
110/71	71	30	55	98/62	69	30	54	99/63	69	29	500	48	254	53	102/70	68	29	
108/70	72	28	49	135/70	95	28	51	121/80	82	27	450	35	330	50	115/76	74	28	

Dexmedetomidine- Group D

2 hr						2.5 hr				3 hr						3.5 hr	
hr	bp	map	psi	dexim	fentanyl	hr	bp	map	psi	hr	bp	map	psi	dexim	fentanyl	hr	bp
	59 97/57	69	28	80	618		57 103/63	69	28		57 92/53	65	27	120	668		55 101/63
	49 108/52	71	28	62.4	720		43 168/74	120	27		48 129/59	84	27	93.6	880		54 120/65
	67 99/64	69	34	56	490		62 92/55	67	27		64 107/65	70	27	84	550		
	52 95/60	67	28	58	281.6		50 100/62	69	28		50 98/63	65	28	92	345.8		50 97/65
	54 112/70	72	29	70	505		53 110/68	71	28		52 110/65	71	28	105	580		52 110/70
	58 110/65	70	30	57	408		54 107/64	70	28		54 108/64	70	28	89	480		
	62 106/62	69	29	46	264												
	50 120/70	89	28	58	334		50 107/60	70	28		50 105/66	70	27	92	388		
	52 135/75	94	28	56	605												
	55 120/80	87	28	56	446		55 130/80	92	28		55 125/70	82	28	82	512		54 120/70
	52 104/70	69	28	54	284												
	52 120/62	84	28	60	526												
	52 122/68	85	28	58	572												
	51 106/70	68	28	60	261												
	57 107/68	69	28	56	390												
	52 124/70	82	28	56	284												
	52 130/67	90	28	76	508		52 124/67	82	28		52 120/71	79	28	112	580		
	52 102/64	67	28	70.5	399		52 105/64	70	27		51 106/64	70	28	103	465		53 105/64
	52 120/68	82	28	103	477												
	52 125/74	84	28	66.4	470		52 120/64	81	28		52 117/73	73	27	96.4	530		52 112/63
	53 120/73	81	28	61	395												
	51 107/62	70	28	60	320		51 101/64	67	28		51 104/65	70	27	90	380		
	52 105/72	68	29	84	326												
	50 115/78	74	28	65	390		50 116/70	73	28		51 117/70	73	28	95	450		

Dexmedetomidine- Group D

4 hr								4.5 hr								5 hr							
map	psi	hr	bp	map	psi	dexim	fentanyl	hr	bp	map	psi	hr	bp	map	psi	dexim	fentanyl
	70	27	55 113/63		73	27	160	728	55 112/64		71	27	63 103/62		69	27	164	778
	79	28	53 97/49		69	27	124.8	940	54 99/50		68	27	52 102/57		68	27	156	1000
	63	28	51 100/78		70	28	120	399										
	70	28	52 111/67		71	28	140	650										
	80	28	54 120/73		79	27	112	578	54 118/76		75	27	54 118/75		74	28	144	644
	69	28	53 106/64		69	27	135.5	531										
	71	27	52 114/73		72	27	120.4	590										

Dexmedetomidine- Group D

Recovery						complications								
respiration	spont mov	extubation	verbal	orientation	icu dischar	bradycardi	tachycardia	hypotensio	hypertensi	respiratory	movement	any injury	new deficit	intraop awareness
30	45	50	55	64	950	1	0	1	1	0	1	0	0	0
45	55	59	61	70	900	1	0	0	1	0	1	0	0	0
25	35	40	42	50	900	0	0	1	0	0	0	0	0	0
45	48	60	65	65	900	1	0	0	0	0	1	0	0	0
50	51	54	56	58	920	0	0	0	0	0	0	0	0	0
30	34	35	36	40	900	1	0	0	0	0	0	0	0	0
27	35	38	41	45	940	0	0	0	0	0	0	0	0	0
25	35	44	47	50	950	1	0	1	0	0	0	0	0	0
35	45	50	54	57	980	1	0	0	1	0	0	0	0	0
45	60	65	70	75	890	1	0	1	1	0	0	0	0	0
15	20	22	24	24	900	1	0	1	0	0	0	0	0	0
25	30	33	35	36	900	1	0	0	1	0	0	0	0	0
25	30	34	36	37	900	1	0	0	1	0	1	0	0	0
15	19	20	22	24	800	1	0	0	0	0	0	0	0	0
28	32	35	36	36	800	0	0	0	1	0	0	0	0	0
25	35	45	47	50	800	1	0	0	0	0	0	0	0	0
30	45	48	50	53	970	1	0	0	1	0	0	0	0	0
40	45	49	50	52	950	1	0	1	0	0	0	0	0	0
22	24	26	27	27	450	1	0	0	1	0	0	0	0	0
50	65	70	72	72	970	1	0	0	1	0	0	0	0	0
30	40	43	44	44	900	1	0	0	0	0	0	0	0	0
35	45	48	49	49	950	1	0	1	0	0	0	0	0	0
20	28	29	30	34	950	1	0	0	0	0	0	0	0	0
20	35	42	46	48	900	1	0	0	0	0	0	0	0	0