REVIEW ARTICLE

Anaesthetic considerations for evoked potentials monitoring

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Abstract

Intra-operative neurophysiologic monitoring (IONM) under anaesthesia has achieved popularity because it helps prevent/minimize neurologic morbidity from surgical manipulations of various neurologic structures. Neurologic functions in an anaesthetised patient can be monitored either by electroencephalography (EEG) or by evoked potentials. Whereas, EEG is difficult to analyse, evoked potentials, in contrast, are easy to interpret, they are either present or absent, delayed or not delayed, with normal or abnormal wave. The goal of IONM is to identify changes in nervous system function prior to irreversible damage. Many factors need consideration when selecting an anaesthetic regimen for intra-operative monitoring of evoked potentials. The very pathophysiological condition or the potential risks of the contemplated surgical procedure, which require evoked potentials monitoring, may place constraints on anaesthetic management as well. With the availability of numerous anaesthetic techniques, an appropriate plan for managing both anaesthesia and IONM in a patient should be organised. It is extremely essential not to alter the pharmacological state of the patient to avoid any changes in the recording of evoked responses. While an anaesthesiologist may alter plans for a patient in order to facilitate IONM, monitoring team too, sometimes may be required to modify plans for monitoring when a particular anaesthetic agent or technique is strongly indicated or contraindicated. At times, compromise may be required between an anaesthesia technique and a monitoring technique. To serve patients' best interest, it is critical to have a team approach and good communication among the neurophysiologist, anaesthesiologist and surgeon.

Key words: Anaesthetics, neurophysiologic monitoring, non-anaesthetic factors

INTRODUCTION

Certain surgical procedures on the central nervous system (CNS) are potentially at risk of damage to the spinal cord or brain. With the use of intra-operative neurophysiology monitoring (IONM), consisting of monitoring of sensory evoked potentials (SEPs) and motor evoked potentials (MEPs), patient's CNS can be examined without requiring patient's co-operation under anaesthesia. IONM facilitates assessment of various neural structures including the cerebral cortex, brainstem, spinal cord, peripheral nerve and neuromuscular junction. Excision of supratentorial lesions closely related to corticospinal tract, clipping of cerebral aneurysm, etc., is also done under IONM. Spinal deformity surgery, which has high potentials of spinal cord trauma, has benefitted most from the IONM. They are equally effective during cervical spine as well as thoracic spine surgery and lumbar laminectomy.[1-3]

Before the introduction of IONM into clinical practice, the surgical team relied on the Stagnara wake up test or ankle clonus to confirm the integrity of spinal cord during procedures potentially risky for the cord. The drawbacks of this test are that they disrupt the surgical procedure, cause mental trauma to the patient and they cannot be performed continually. Moreover, sudden movement of the patient during these tests might produce damage to the cord.[4,5] IONM avoids all these disadvantages

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while monitoring the integrity of the spinal cord. SEPs differ in their sensitivity to anaesthetic agents depending upon the neurologic pathways involved and the specific anaesthetic agents used.[6] Whereas, visual evoked potentials (EPs) are the most sensitive to influence of anaesthetic agents, the brainstem EPs are least sensitive and somatosensory evoked potentials (SSEPs) are intermediate in their sensitivity to the anaesthetic agents.

Injury to the nervous system can occur at multiple levels and may involve multiple pathways. Because the spinal MEPs and SSEPs pathways have different arterial supplies (the anterior and posterior spinal arteries, respectively), it is possible to injure the motor tract without its detection, during spinal surgery, when monitoring with SSEPs alone. Because of this possibility, MEPs monitor the motor pathways of the anterior cord. However, it is unusual to produce motor tract injury when SSEPs remain unchanged.[1] Therefore, to assess CNS integrity comprehensively, both SSEPs and MEPs should be monitored simultaneously. MEP monitoring is extremely challenging as they are easily suppressed by anaesthetic agents.

ANAESTHETIC EFFECTS ON SENSORY AND MOTOR PATHWAYS

The impact of inhalational anaesthetic agents on neurophysiological monitoring is directly proportional to the number of synapses in the pathway monitored because they act mainly by changing the neuronal excitability through changes in synaptic transmission rather than on axonal conduction.[7] More number of synapses in the pathway may explain why cortically generated EPs are more sensitive to anaesthetics than subcortical signals. For example, visual EPs represent cortical activity and are therefore, highly sensitive to the anaesthetics while brainstem auditory EPs, which represent brainstem and subcortical activities, are the least sensitive to anaesthetic effects. Intra-venous anaesthetics act primarily by enhancing the inhibitory functions of gamma amino butyric acid and increase the chloride conduction, membrane hyperpolarisation and producing synaptic inhibition.[8]

Ketamine appears to act by blocking N-methyl-D-aspartate receptors. This leads to reduction of sodium as well as calcium flux inside the cells.[9] Similarly, most anaesthetic agents interact at multiple receptors in many pathways such that the effect on evoked responses likely varies with the spectrum of specific receptors and pathways influenced. For example, barbiturates up-regulate the N-methyl-D-aspartate receptor and interact competitively with some of the other binding sites.[8]

Opioids activate mu, kappa and delta opioid receptors. Their mechanism of action is by increasing inward potassium currents and decreasing outward sodium current. This explains why opioids have little, if any, influence on evoked responses.

The effects of anaesthetic agents are thus the result of direct inhibition of synaptic pathways or by indirect effect on pathways by altering the balance between inhibitory and excitatory influences. Ketamine and etomidate belong to the latter category Thus, while all other anaesthetic agents depress amplitude and increase the latency, ketamine and etomidate increase the amplitude perhaps by attenuating inhibition.[10] Thus, the electrophysiologic responses that rely excessively on synaptic function will be most susceptible to anaesthetics. This explains why cortical responses are more sensitive to anaesthesia than those generated in the periphery such as brainstem or spinal cord, where lesser number of synapses is involved.[10]

Criteria for Significant Change in Sensory Evoked Potentials

SEPs responses being very low in amplitude require prolonged averaging. Therefore, it may take 3-5 min to determine a significant change depending on the ambient noise level. Injury to the large fibre dorsal column pathways is typically expected with more than 50% decrease in the amplitude or 10% or more increase in latency or both, provided these changes are not caused by anaesthetics or temperature changes.[11] At least one study suggests that the use of amplitude criteria is associated with better sensitivity for detecting neurologic injury than latency criteria.[12] The SSEPs are thought to have high specificity and low sensitivity to injury.

Criteria for Significant Change in the Myogenic Motor Evoked Potentials

One criterion is the threshold criterion proposed by Calancie *et al*.[13] The criterion was based on the fact that stimulus threshold for obtaining a muscle MEP increases when there is damage to the corticospinal tract. Typically, increase of more than 100 V in the threshold for obtaining a muscle MEP is considered an early sign of injury. The difficulty with this criterion is that thresholds generally increase gradually during surgery and are significantly influenced by even small change in anaesthesia.[14] Another criterion, which is often used, is complete abolition of muscle MEPs. Clearly, this indicates a significant change, but it does not always indicate a permanent injury. Other investigators have proposed that a decrease in amplitude of more than 50% should be considered as significant.[15] The drawback with this criterion is that there is some natural variability in the muscle MEPs, which may introduce the false positive and false negative outcome. Spinal MEPs (i.e., D waves, recorded by insertion of epidural electrodes) are more robust to influence of anaesthetics compared with myogenic MEPs. However, the biggest problem of spinal MEPs is that, with the onset of ischaemia, they disappear

gradually compared with myogenic MEPs, therefore, do not permit quick intervention. Other drawback is that they are invasive in nature.

PRE-EXISTING DAMAGE TO THE MOTOR PATHWAYS AND THE TRANS-CRANIAL MOTOR EVOKED POTENTIALS

It is imperative to note that the condition of the motor pathways before surgery is extremely critical to the generation of muscle MEP. In presence of any pre-existing injury, even if patient has good muscle power pre-operatively, it may not be easy to get MEPs recording. The reason for this is that the activation of anterior horn cell needs a highly synchronised volley of inputs that loses synchronisation easily even by a minor disruption of conduction.

Action of Various Anaesthetic Agents on Evoked Potentials

All halogenated agents result in dose dependent increase in latency and decrease in amplitude of the cortical SSEPs [Table 1]. However, recordings from cervicomedullary junction, spinal cord or peripheral nerve result in amplitude decrease and latency increase of lesser degree as compared with cortical recording. In this respect, isoflurane is the most potent suppressant while halothane is the least.[10]

Satisfactory monitoring of early cortical SSEPs is possible with 0.5-1.0 minimum alveolar concentration (MAC) halothane or isoflurane without nitrous oxide.[16] Addition of nitrous oxide potentiates the depressant effects of volatile agents. For equal MAC concentration, inhalational agents result in greater signal depression.[17] The newer anaesthetic agents, sevoflurane and desflurane, affect SSEPs not unlike isoflurane; but may permit the use of higher inhaled concentration. Increase in latency and decrease in amplitude occurs at doses of 1.5 MAC of sevoflurane and desflurane or less, with minimal effect on subcortical SSEPs.[18] Studies with sevoflurane and desflurane suggest that they are similar to isoflurane at a steady state, however, because of their rapid onset and offset of action, they may appear to be more potent during period when concentration is increasing.[17]

Table 1: Effect of various anaesthetic agents on evoked responses

Anaesthetic agent	SSEP	MEP
Halothane (0.5-1 MAC)*	↓A ↑ L	++
Isoflurane (0.5-1 MAC)*	↓A ↑ L	++
Sevoflurane (1.5 MAC)*	↓A ↑ L	++
Desflurane (1.5 MAC)*	↓A ↑ L	++
Nitrous oxide (60-70%)	↓A −L	++
Barbiturates	↓A ↑ L	++
Propofol	↓A	++
Ketamine	↑A	+
Etomidate	↑A	+
Opioids	↓A ↑ L	−
Benzodiazepines	−	+++
Dexmedetomidine	−	+
Neuromuscular blockers	−	+++

MAC = Minimum alveolar concentration, SSEP = Somatosensory evoked potential, MEP = Motor evoked potential, A = Amplitude, L = Latency, − = Negligible or no effect, + = minimal effect, ++ = significant effect, +++ = Profound effect, *without nitrous oxide

Since the threshold of anaesthesia effects on cortical sensory and peripheral myogenic responses may vary in some patients, any amount of inhalational agent may be unacceptable during IONM, necessitating a total intra-venous anaesthesia (TIVA). This is especially common if patient has compromised in the neural pathway from some pathology or immaturity (e.g., patients aged below 3 years). In the latter cases, an amplitude enhancing agent (like ketamine or etomidate) may be infused to reduce those components of TIVA, which depress responses.

The effects of volatile anaesthetics on cortical SSEPs amplitude are complicated by nitrous oxide. Increasing isoflurane from 0.5 to 1.0 MAC in the presence of nitrous oxide leads to a 75% depression of cortical SSEPs.[19]

Myogenic MEPs are easily abolished by halogenated volatile anaesthetic agents. The easy abolition of single pulse stimulation myogenic trans-cranial MEPs (TcMEPs) is shown by the fact that they become un-recordable in the presence of inhalational agents. However, recording is possible only at low concentrations, for example at 0.2-0.5% of halogenated agent. The effect is likely due to depression of synaptic transmission either in the anterior horn cell synapses on the motor neurons or in the cortex on the internuncial synapses with loss of indirect (I) wave.

Direct (D) wave being resistant to volatile agents, the anaesthetic effect at the anterior horn cell can be overcome at low anaesthetic concentrations by high frequency (multiple pulse) trans-cranial stimulation (train of stimuli with inter-stimulus intervals of 2-5 ms). With this technique, the multiple D waves (and I waves, if produced) summate at the anterior horn cell to generate a peripheral nerve action potential and subsequent myogenic response. However, the best anaesthetic technique is to avoid inhalational agents altogether for satisfactory MEP recording even when using high frequency stimulation technique.[20]

Even if paired impulses or train of pulses are employed for motor cortex stimulation, they cannot overcome the suppressive effects of inhalational agents on MEPs.[21]

Although the exact site at which myogenic MEPs are suppressed by inhaled anaesthetics is unclear, synaptic transmission has been postulated to be the primary site of the volatile agents. Zentner *et al*., suggested that the descending impulse elicited by electrical stimulation of the motor cortex during anaesthesia with volatile agents was inhibited mainly at the level of the spinal inter-neuronal of motoneuronal systems.[22]

Notwithstanding the recommendation against certain volatile anaesthetics, muscle MEPs can be recorded in the presence of low concentration of isoflurane, sevoflurane and desflurane and/or low concentration of nitrous oxide. The clinical question relating to the use of these agents during monitoring is, 'When there is change in the muscle MEP, can the monitoring team be certain that the change was not induced by anaesthetic'? This is a complex but pertinent question because the effects of the inhalational agents on EPs are not simply related to the end tidal concentrations of the agents, but also on other factors such as the time over which the anaesthetic has been delivered and presence of pre-existing nervous tissue injury. It is much safer not to waste precious time answering this question when there is an intra-operative change, and therefore, avoid altogether inhalational agents including nitrous oxide.[23]

EFFECTS OF NITROUS OXIDE ON EVOKED POTENTIALS

Nitrous oxide (60-70%) decreases the cortical amplitude by about 50%, but does not alter the cortical latency and subcortical waveform.[19,24] It potentiates the depressant effects of volatile and most intra-venous anaesthetics.[25-27] At equipotent concentration, nitrous oxide causes more profound changes in cortical SSEPs than any other volatile agent.[10] Like volatile agents, effects on subcortical sensory responses are minimal [Table 1].

Nitrous oxide has been used during MEP studies in combination with other anaesthetics, even despite its suppressant action on MEPs. Woodforth *et al*., recorded myogenic MEPs in response to single pulse stimulation in patients anaesthetised with fentanyl and 70% nitrous oxide, although MEP amplitudes were very low.[28] Zentner *et al*., demonstrated that with 60% nitrous oxide, there was reduction of amplitude of single pulse trans-cranial stimulation to less than 9% of the baseline value in healthy volunteers.[29] Jellinek *et al*., suggested that nitrous oxide should be given in less than 50% concentration, if used as an anaesthetic adjunct for MEP monitoring during propofol TIVA.[30]

The effect of nitrous oxide on myogenic MEPs in response to stimulation with paired or train of pulses is controversial, some studies show that although amplitude is reduced, they can still be recorded even with 60% concentration, while other studies have shown that 50% nitrous oxide did not alter the amplitude of MEPs induced by trans-cranial electrical stimulation with paired pulses during fentanyl and low dose propofol anaesthesia.[31] Sakamoto *et al*., observed that application of a train of five impulses could reverse the nitrous oxide-induced suppression of MEPs, in the absence of propofol infusion and during low dose propofol infusion. However, during high dose propofol administration, nitrous oxide significantly suppressed MEPs, regardless of the stimulation paradigm. This suggests that nitrous oxide-induced suppression of MEPs could be modified by the use of multiple stimulation and administration of propofol. When nitrous oxide is used as supplement, high dose propofol should be avoided.[32]

EFFECTS OF BARBITURATES ON EVOKED POTENTIALS

Immediately following induction with thiopentone there is transient decrease in amplitude and increase in latency of cortical sensory responses [Table 1]. The effect lasts less than 10 min.[27] Minimal effects are seen on subcortical and peripheral responses. This is consistent with the fact that barbiturates, like volatile anaesthetics, influence synaptic transmission more than axonal conduction.

MEPs exhibit unusual sensitivity to barbiturates with prolonged effect. Induction bolus may abolish myogenic from MEPs for 45-60 min.[33] It is not known if multi-pulse stimulation can overcome this suppression of myogenic MEPs. Therefore, commendation is to avoid barbiturates during the intra-operative monitoring of MEPs.

EFFECTS OF PROPOFOL ON EVOKED POTENTIALS

Propofol decreases the amplitude of cortical responses with quick recovery on termination of infusion.[34] When used as a sedative hypnotic in combination with opioids, propofol reduces amplitude lesser than nitrous oxide or midazolam.[35] Propofol use results in higher cortical SSEP amplitude despite, the use of anaesthetic concentration equivalent to nitrous oxide or sevoflurane.[36] As a component of TIVA, infusion of propofol in combination with an opioid has achieved popularity and produces acceptable conditions for monitoring of cortical SSEPs.[37] Because it is very easy to titrate the dose rapidly, propofol has become an extremely popular agent in TIVA.

Propofol is powerful suppressant of MEPs induced by single pulse stimulation.[34] As a component of TIVA, propofol provides acceptable conditions for MEPs recording.[20,37] Although MEPs induced by single pulse stimulation are suppressed, they can be recorded when

a train of pulse is used for stimulation. Pechstein *et al*., compared isoflurane and nitrous oxide combination with propofol anaesthesia for MEPs recording after multi-pulse stimulation and demonstrated that the latter was superior to this inhalational combination for intra-operative MEP recording.[20] Therefore, propofol-based TIVA has become the standard anaesthesia technique for intra-operative recording of myogenic MEPs.

EFFECTS OF KETAMINE ON EVOKED POTENTIALS

Ketamine can enhance cortical SSEP amplitude.[38] It has minimal effects on subcortical and peripheral SSEP responses [Table 1]. Because of these properties, ketamine is a useful agent for eliciting responses that are usually difficult to record under anaesthesia. Its maximum effect on amplitude is observed within 2-10 min after bolus administration.[39] It can be used to decrease the dose of other depressants in TIVA (e.g., propofol), or as the sole sedative agent with resultant increase in SSEPs in children.[40] However, increase in intra-cranial pressure in presence of cerebral pathology post-operative hallucinations, increase in blood pressure, etc., may limit the use of ketamine in certain conditions. Incidence of such adverse effects are reduced remarkably when it is low dose propofol (1-3 mg/kg/h) is infused as a supplement.[41]

Ketamine is shown to have little effect on MEPs.[42] Kalkman *et al*., demonstrated that 1 mg/kg ketamine did not cause significant changes of magnetic MEPs in volunteers.[43] Therefore, ketamine is a useful anaesthetic agent during monitoring of myogenic MEPs, especially in presence of pre-operative motor dysfunction where use of anaesthetic agents with suppressive effects on MEPs may make intra-operative monitor difficult or impossible.

EFFECTS OF ETOMIDATE ON EVOKED POTENTIALS

Like ketamine, etomidate too increases the cortical SSEP amplitude, up to 400% above pre-induction baseline in some patients.[27] Subcortical amplitude is decreased by 50% [Table 1]. Etomidate leads to high incidence of myoclonic movements.[44] Patients of familial myoclonus epilepsy are known to show abnormally high EP responses, especially during myoclonic jerking episodes.[45] However, these myoclonic episodes are not responsible for enhanced SSEP amplitude, because such increased amplitude is also noted in the absence myoclonus.[46] From animal studies, it appears that etomidate enhances amplitude from an altered balance between inhibitory and excitatory influences at cortical level, resulting in increased signal synchronisation at the thalamic level.[47,48] However, transient increase in amplitude of SSEPs (injury current) may represent an early warning sign of CNS hypoxia[49] and etomidate, theoretically could interfere with early detection of CNS hypoxia.[50] However, Sloan *et al*., observed that it did not mask neural tissue ischaemia.[51]

Like its enhancement effect on SSEPS, etomidate also increases the amplitude of MEPs.[46] Thus, it has been used for induction and a component of TIVA for maintenance of anaesthesia.

EFFECTS OF OPIOIDS ON EVOKED POTENTIALS

Because they alter SSEPs minimally compared with inhalation agents, opioids (fentanyl, remifentanil, sufentanil) have become a popular component of TIVA. They cause little changes in spinal and subcortical SSEP recording. There is slight reduction in cortical amplitude and increase of latency in the late cortical responses (latency more than 100 ms) [Table 1]. The effect of bolus fentanyl and also bolus morphine is greater than continuous infusion.[52] Compared with combination of fentanyl and nitrous oxide, remifentanil reduces cortical amplitude less, with lower amplitude variability.[53] A recent study observed that remifentanil produced dose dependent (0.8 μg/kg/min) decrease in amplitude of SSEPs, in some patients even over 50%, however, increase in latency was not significant. Therefore, the authors suggested that if high dose remifentanil infusion is contemplated, it should be combined with other agent, in order to titrate remifentanil to a smaller dose.[54] Administration of subarachnoid meperidine produced a 60% drop in cortical posterior tibial nerve SSEP amplitude and a 10% increase in latency. The response was abolished in 40% of patients.[55] Meperidine acts by its local anaesthetic-like effect from blockage of voltage-dependent sodium channels. In contrast, opioids deposition in subarachnoid space have no effects on SSEPs.

They decrease the amplitude and increase the latency only slightly. Kalkman *et al*., reported no significant alterations in MEPs with a single pulse after intra-venous bolus administration of 3 μg/kg fentanyl.[34] Even 8 μg/kg did not influence MEPs amplitude in response to trans-cranial magnetic stimulation in humans.[56] In contrast, by decreasing the background spontaneous muscle contractions and associated motor unit potentials, fentanyl improves the myogenic responses.

EFFECTS OF BENZODIAZEPINES ON EVOKED POTENTIALS

Midazolam in induction doses (0.2 mg/kg) in absence of any other agent, results in slight depression of cortical

SSEP amplitude and minimal effect on subcortical and peripheral components[57] [Table 1]. Adding opioid or nitrous oxide to midazolam preserved the cortical SSEPs better when compared with adding nitrous oxide or opioids to thiopentone or etomidate.

Midazolam suppresses the effects of myogenic MEPs. Even 0.05 mg/kg caused a significant decrease of MEPs in response to trans-cranial electrical and magnetic stimulation to 23% and 16%, respectively, of the baseline values in humans.[34] The suppression may be prolonged, therefore, making midazolam a poor induction agent when MEP recording is planned.

EFFECTS OF DEXMEDETOMIDINE ON EVOKED POTENTIALS

Dexmedetomidine as an adjuvant to desflurane and remifentanil anaesthesia, at target plasma concentration of up to 0.6 ng/ml does not change SSEPs or MEPs response during complex spinal surgery by any clinical significant amount[58] [Table 1]. Mahmoud *et al*., described two case reports of dexmedetomidine induced suppression of TcMEPs with gradual recovery after sometime.[59]

EFFECTS OF NEUROMUSCULAR BLOCKING AGENT ON EVOKED POTENTIALS

They do not have any direct influence on SEPs [Table 1]. However, by reducing the noise in recording electrodes, they may improve waveform quality by favourably increasing the signal-to-noise ratio by abolishing the electromyography artefact.[60] In presence of deep neuromuscular blockade it is not possible to record compound muscle action potential (CMAP). However, partial neuromuscular blockade not only has the benefit of attenuating the patient movements caused by motor stimulation, but it also facilitates the surgical procedure because muscle relaxation aids surgeon for dissection and retraction of muscles. Neuromuscular block is conventionally assessed either by measuring the twitch height (T1) or by train of four (TOF) response. Successful monitoring of myogenic responses has been accomplished at T1 between 5% and 50%. Dongen *et al*., investigated the effects of levels of neuromuscular blockade (T1 response, 5-15% vs 45-55%) on the within patient variability and amplitude of myogenic MEPs and demonstrated that, although MEP recording was feasible with a T1 response of 5-15%, larger and less variable MEPs were recorded at a T1 response of 45-55% than at 5-15%.[61] Thus, a stable neuromuscular blockade at 45-55% of baseline could provide reliable and recordable muscle responses during the intra-operative recording of myogenic MEPs. Effective monitoring has been performed in the presence of two of the four twitches of TOF.[17]

When using muscle relaxant, keep the blockade under tight control, so as to avoid excessive blockade and thereby, eliminating recording, which mimics a nerve injury. In order to keep blockade within a narrow range, the use of a closed loop continuous infusion of a relaxant is recommended. Because of varying muscle sensitivity to muscle relaxants, the blockade should be evaluated in the specific muscle groups used for electrophysiological monitoring.[17]

As a consequence of amplitude decrease, the ability to record with incomplete muscle relaxation will depend upon other factors like anaesthesia that may influence to reduce amplitude, neurologic disease or other drugs (like magnesium or alpha 2 receptor antagonists), which the patient may be taking.[62] Therefore, amplitude reduction with pre-existing small response or other factors, which reduce the amplitude, may make the use of muscle relaxant more difficult. Fortunately, the CMAP amplitude is usually quite large. It is pertinent to note that the use of amplitude criteria for warning the impending motor nerve injury may not be possible because inevitable fluctuations in the degree of blockade may obscure the application of these strict criteria. Because of this reason, some neurophysiologists use only presence or absence of a response rather than amplitude criteria.[17]

NON-ANAESTHETIC INTRA-OPERATIVE FACTORS AFFECTING EVOKED POTENTIALS

Blood Flow and Blood Pressure

There is a threshold relationship between regional cerebral blood flow and cortical evoked response.[10] The cortical SSEPs responses are unaffected until blood flow is decreased to 20 ml/min/100 g. Between 15 and 20 ml/min/100 g blood flow, the SSEPs are affected and finally lost. Like effects of anaesthetics, subcortical responses seem to have lower sensitivity than cortical ones to reduced blood flow.

Even in the presence of normal systemic blood pressure, local factors may cause regional ischaemia. In spinal surgery, the effects of hypotension may get aggravated by spinal distraction, such that an acceptable limit of systemic hypotension cannot be determined without monitoring.[63] Similarly, peripheral nerve ischaemia can result from positioning, torniquet, carotid artery interruption, vertebrobasilar insufficiency aggravated by head extension, cerebral vasospasm and cerebral ischaemia from retraction. MEPs and SEPs may depict differential sensitivity to an ischaemic episode during

reduced blood flow to spinal cord, although both are altered following thoracic aorta clamping decreasing spinal cord blood flow.

A reduction in blood pressure below autoregulation threshold progressively decreases SSEP amplitude without changing latency. Such changes may be reversible or irreversible, depending upon the severity of reduction of blood pressure. A rapid decrease in mean arterial pressure within the autoregulatory range is also associated with transient change in amplitude of SSEPs that resolves. Haemorrhagic shock is associated with a transient increase in the amplitude of SSEPs probably related to the phenomenon of anoxic activation followed by decreased amplitude and loss of SSEPs.[64]

Hypoxia

Mild hypoxia ($PETO_2$ of 48 mmHg) does not influence human SSEPs.[65] Severe progressive hypoxia is associated with a decrease in SSEP amplitude and increase in latency ultimately leading to complete loss of cortical SSEPs.[66] Cortical SSEPs are more sensitive than spinal and subcortical responses, presumably because the latter are more tolerant of hypoxia than cerebral cortex, because of their lower metabolic rate.[67] Early response to ischaemia or hypoxia can manifest as a transient increase in SSEP amplitude (injury potential) before amplitude decreases and latency is prolonged. This may be related to the phenomenon of anoxic activation, which is attributed to early loss of function by inhibitory cortical neurons.

Intra-cranial Pressure

Increased intra-cranial pressure leads to reduction of amplitude and increase in latency of cortically generated SSEPs.[68] Raised intra-cranial pressure, perhaps affects the cortical structures, thereby, causing a pressure-related reduction in cortical responses. Loss of brainstem responses results with the onset of uncal herniation. As for MEPs, there is gradual increase in onset of response until it can no longer be produced.[17]

Blood Rheology

In experimental animals, Nagao *et al*., observed an increase in amplitude with mild anaemia and increase in latency at haematocrit of 10-15%. They observed further changes in latency and amplitude with haematocrit below 10%. These changes were partially restored when haematocrit was raised.[49] There is no study on effects of haemodilution on MEPs.

Carbon Dioxide

Hypocapnia 20-25 mmHg shortens latency by 2-4% in awake volunteers as well as in isoflurane anaesthetised patients.[69] In contrast to the 70% cortical amplitude enhancement seen in hyperventilating awake volunteers,[65] no change in amplitude enhancement took place in anaesthetised hypocapnic patients.[69] The hypocapnia-related decrease in latency reflects an increase in conduction velocity, probably attributed to alteration in pH, ionised calcium levels, etc., enhancing neuronal excitability. It does not seem to be related to alteration in anaesthetic depth.[65] In contrast, hypercapnia to a level of 50 mmHg had no effect on human SSEPs.[70] However, greater than 100 mmHg carbon dioxide levels in animals resulted in increase in latency by 15-30% and decrease in amplitude by 60-80%.[71] Levels below 20 mmHg may result in ischaemia from vasoconstriction and lead to significant SSEPs changes. This has been suggested to contribute to changes in SSEPs during spinal surgery and may be expected to produce some MEP alterations.[72]

Temperature

To assess the relationship between SSEPs and body temperature, the site of temperature monitoring is important. In patients undergoing hypothermic cardiopulmonary bypass, posterior tibial nerve SSEP latency correlated best with nasopharyngeal temperature. Hypothermia to 35°C decreased central and peripheral nerve conduction velocities, SSEP latency and central conduction time increased by 10-20%. These changes in SSEPs induced by hypothermia return to baseline after 30 min of re-warming.[73] While hypothermia induced alterations of SSEP latencies are well-defined, amplitude behaves in an un-predictable manner.[74] Pathological prolongation of SSEP latency can be presumed if latencies increase substantially beyond the level predicted by temperature changes (1.5 ms/°C for early cortical SSEPs), particularly if asymmetric changes are detected.

Nitrous oxide should be used with care because it markedly suppresses MEPs under hypothermia.[75] Hypothermia may also change the plasma concentration of anaesthetics and neuromuscular blockade and therefore, influence the MEPs. Leslie *et al*., demonstrated that a temperature reduction of 3°C increased blood porpofol concentration by 30% during constant rate of infusion.[76]

Regional temperature changes can also alter evoked responses that would not be otherwise predicted based on unchanged core temperature. Irrigation of spinal cord, brainstem, etc., with cold saline causes routine alterations in evoked responses. For the same reason, limb cooling (from cold infusion of fluids) can change the SSEP originating from stimulation to a nerve from that extremity.[17] Hypothermia also increases stimulation threshold.

SAFETY AND COMPLICATIONS OF MOTOR EVOKED POTENTIALS

Electric Shock

Because of high voltage (600-900 V) and high current delivered during trans-cranial stimulation, there is risk

of tissue injury or shock to the operation room personnel who inadvertently comes in contact with stimulating electrode during stimulation.[23]

Bite Injuries

The spread of current during trans-cranial stimulation can cause direct stimulation of trigeminal nerve, causing jaw contractions. The most common, but infrequent complication of trans-cranial MEPs is the bite injury of tongue or lips, and has incidence of 0.2%.[77] Most of such injuries heal spontaneously, but rarely surgical intervention has been required. Mandibular contractions may result in patient biting through the endotracheal tube creating an emergency. Do not insert a hard bite block because of the risk of damage to teeth. An effective approach is to make two large cotton wads from 4 × 4 inches gauze pieces and insert them bilaterally between the molars on each side.

Movement-induced Injuries

The patient may move during the elicitation of trans-cranial MEPs injuring a vital structure if it is jolted or torn away. However, there is currently no reported incidence.[77] This risk is particularly important during brain surgery. It is prudent on the part of monitoring team to intimate the surgeon immediately prior to a stimulus.

Seizures

The possibility that brain stimulation could provoke a seizure is always there. It is recommended not to give stimulation very frequently in patients at risks of seizures.[23] The risk is tiny for seizure with pulse train stimulus transcranial electrical stimulation, fortunately without morbidity so far.[77] Their rarity makes it uncertain what proportion is due to stimulation or anaesthesia that can also induce seizure rarely.[77]

Cardiovascular Complications

Cardiac arrhythmias or blood pressure changes have been observed rarely during pulse train TES, but relationship, if any, is unclear.[77] Current penetration to the hypothalamus or brainstem is one possible mechanism. Trans-cranial electrical stimulation artefact may mimic cardiac arrhythmias. In presence of implanted defibrillator, it is prudent not to perform the study unless there is very high risk of motor injury. In that case, consultation in advance with a cardiologist is suggested. For patients with a pacemaker without defibrillator, although the risk of damage or aberrant firing of the pacemaker is low, the issue should be discussed with a cardiologist.[23]

CONTRAINDICATIONS TO TRANS-CRANIAL ELECTRICAL MEPS

Relative contraindications to TcMEP stimulation include epilepsy, convexity skull defect, cortical lesions, raised intra-cranial pressure, cardiac disease, proconvulsant medications or anaesthetics, intra-cranial electrodes, vascular clips or shunts and cardiac pacemakers or other implanted biomedical devices.[77] In an infant with open fontanelle or open suture do not use spiral needle electrode.[78]

ANAESTHETIC CHOICE AND MANAGEMENT

Always create a stable anaesthetic environment prior to recording a baseline signal and do not alter anaesthetic technique (including depth of anaesthesia) throughout the procedure. Haemodynamic parameters should not be manipulated with anaesthetic agents, but with vasoactive drugs.[79] To maintain constant depth of anaesthesia seems easy, but in practice, it is highly difficult to achieve. A satisfactory plan of anaesthesia in the early phase of surgery requiring muscle dissection may become insufficient during instrumentation. Therefore, surgeon may demand muscle relaxants during the dissection phase and relaxant may be given during this phase of surgery, but ensure that prior to instrumentation, the effect of relaxant has dissipated and normal motor signals have returned satisfactorily. A bolus administration of an intra-venous anaesthetic will result in complete signal loss during a critical phase of surgery. Choose an anaesthetic agent with rapid onset of action and minimal effect on evoked responses. It is extremely imperative to convey the monitoring team of any change in the anaesthetic technique or bolus administration. It must be understood that anaesthesia would result in global signal loss; whereas, trauma will be limited to the specific surgical area. Recovery of lost signal from surgical trauma and anaesthesia technique may take 30 min or even longer. During this period, absence of signals would pre-dispose a patient to surgical injury without any warning.[79] Additionally, structure with poor baseline signals may be more difficult to monitor because it may be more affected by anaesthetics. According to Deiner *et al*., diabetes, hypertension and anaesthetic techniques are the most important risk factors associated with failure to obtain lower extremity MEP signals.[80]

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