Original Article

Transcranial motor evoked potential monitoring outcome in the high-risk brain and spine surgeries: Correlation of clinical and neurophysiological data – An Indian perspective

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Abstract

Objective: The objective of this study is to assess the safety, feasibility and clinical value of transcranial motor evoked potential (MEP) monitoring by electrical stimulation. **Setting:** Clinical neurophysiology department of tertiary reach hospital. **Materials and Methods:** MEP monitoring was attempted in 44 "high risk" patients. Intraoperative surgical, anesthesia and neurophysiological findings were documented prospectively. MEP monitoring results were correlated with motor outcome. **Results:** The success for reliable MEP recording from the lower limbs was 75%. Incidence of new permanent post-operative motor deficit was zero. Nearly, 76.5% of the cases (13 out of 17 cases) who showed unobtainable and unstable MEP outcome had lesion location in the spine as compared with 23.5% (4 out of 17 cases) that had lesion location in the brain. Chi-square test demonstrated a statistically significant difference between these two groups ($P = 0.0020$). Out of these 13 spine surgery cases, 8 (62%) were operated for deformity. Seven out of 12 (60%) patients less than 12 years of age had a poor MEP monitoring outcome suggesting that extremes of age and presence of a spine deformity may be associated with a lesser incidence of successful MEP monitoring. No complications related to the repetitive transcranial electrical stimulation for eliciting MEP were observed. **Conclusion:** MEP monitoring is safe. The protocol used in this study is simple, feasible for use and has a fairly high success rate form the lower limbs. Pediatric age group and spine lesions, particularly deformities have an adverse effect on stable MEP recording.

Key Words

Clinical and neurophysiological correlation, high-risk cases, motor evoked potential

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Introduction

Intraoperative neuromonitoring is being increasingly embraced by the surgeons for brain and spine surgeries to improvise on surgical outcomes. Somatosensory evoked potentials (SSEPs) have been used for more than 20 years beginning with scoliosis surgeries. SSEP monitoring is specific only to the ascending posterior columns of the spinal cord. The proximity of sensory pathways to motor pathways was the basis of SSEP recording to detect loss of integrity of motor pathways. However, the limitation of SSEP monitoring is that it is not completely reliable to monitor functional integrity of the motor pathways and also the inherent delay due to averaging of responses.[1] Therefore, SSEP monitoring for motor integrity has shown a high false-negative rate.[2,3] Motor evoked potentials (MEP) can be reliably evoked by transcranial stimulation of the motor cortex. Myogenic responses are recorded in the form of compound muscle action potential (CMAP) from the distal muscles of the limbs using the needle electrodes. The stimulation of the motor cortex causes depolarization of the pyramidal neurons, which is then conducted down the pyramidal tract and ventral columns of the spinal cord. MEP is now the preferred method for monitoring of motor pathways as it correlates well with the outcomes.[4]

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For several years, various centers have used transcranial MEP recording during surgery to avoid permanent neurologic injury resulting from surgical manipulation.[4,5] There are no randomized control trials showing a favorable surgical outcome with the use of intraoperative neuromonitoring. However, there is enough evidence that it is a very useful adjunct to prevent neurological injury related to surgical procedures. Multimodality evoked potential monitoring has become a standard of care during spine surgery.[6,7] However, in the Indian setting no such series has been published to date. In an attempt to establish the feasibility, safety and clinical application of MEP recording in high-risk surgeries, 44 patients were prospectively evaluated in this study.

Materials and Methods

Patient data

In January 2009, a pro forma was created to address the need for intraoperative MEP monitoring during high-risk brain and spine surgeries. An expected enrollment of 10-15 patients per year was proposed and enrollments were proposed to close by February 2013. The outcome to be assessed was the development of a new permanent post-operative deficit. Consent for MEP was obtained together with the consent for the surgery.

Patients were grouped for age as; 30 patients were in the 12-60 years age group, 12 were less than 12 years of age and 2 were more than 60 years of age. Age ranged from 5 days to 75 years. 24 were male and 20 were female. The duration of monitoring ranged from 3 to 10 h, average duration of 3.6 h. A total of 12 patients required surgery for brain lesions and 32 for spine lesions.

The number of patients for the various diagnoses requiring monitoring during the surgery is shown in Table 1.

MEP monitoring protocol

Transcranial electrical stimulation technique was used. Nicolet endeavor CR monitoring system was used. Stimuli were delivered through subdermal needle electrodes placed at C3 and C4 (International 10-20 system of electroencephalogram electrode placement system). Stimuli were delivered in trains of 5 stimuli at 500 Hz; up to 400 V in intensity. The train duration was 300 μs. Subdermal needle electrodes were used for recording CMAPs in the target muscles.

Usually, the tibialis anterior, gastrocnemius and quadriceps femoris were recorded supplemented in a few patients with hand and foot muscles and the anal sphincter. In this series, tibialis anterior was monitored along with other muscles in all cases as post-operative foot drop was a concern.

Depending upon the site of the lesion and or craniotomy, recording from all extremities was either not possible or not necessary. Responses were taken at baseline after anesthesia and before skin incision, after dural opening or spine exposure and at critical surgical stages. The parameter monitored was the complete disappearance of MEPs.[5,8]

Anesthesia considerations

Neuromuscular blocker was used for induction in all patients and was to be preferably avoided thereafter. However, four patients received maintenance infusion of muscle relaxants on request of the anesthetist. Most commonly used maintenance agents were propofol, ketamine, midazolam, dexmedetomidine and up to 0.5 MAC sevoflurane.[9]

Results

As a part of multimodality intraoperative monitoring, MEP was used in 44 cases. The success for reliable MEP recording from the lower limbs was 75% (33 out of 44 cases). The results of MEP monitoring with respect to age, presence of pre-operative deficit, use of muscle relaxant during maintenance anesthesia and lesion location is shown in Table 2. Unobtainable MEP (failed MEP) was observed in 11 cases. Out of the 33 cases where the MEP was reliably obtained, 27 cases had stable responses in all or more than half the number of target muscles. In 6 cases, the responses were present in less than half the number of the target muscles (unstable MEPs) but were consistent. When the unobtainable MEP and unstable MEP group were combined, 17 patients had poor MEP monitoring outcome. There was no incidence of intraoperative seizure, which could have led to cessation of MEP recording. New post-operative deficit was not observed in any case.

Stable MEPs appeared to be affected by age [Figure 1]. The MEP monitoring in the 12-60 years age group had a success rate up to 78%. When the unstable and unobtainable MEP groups were combined; 7 out of 17 patients (60%) were under 12 years of age. Of these, 3 were less than 5 years of age.

Nearly, 41.7% of the cases who were in the age group of less than 12 years had unobtainable MEP outcome, which appears to be significantly more as compared with 18.8% of the cases

Table 1: Numbers of patients for the various diagnosis undergoing MEP monitoring during surgery

Brain tumor	12
Scoliosis	13
Spinal tumor	9
Spina bifida	5
Cervical and lumbar spondylosis	3
Spine fracture	1
Atlantoaxial dislocation	1

MEP=Motor evoked potential

Table 2: Correlation of MEP recording with age, presence of pre-operative deficit, use of muscle relaxant infusion during the surgery and lesion location

MEP outcome	Age (year)			Pre-operative deficit	NMB	Lesion location	
	<10	10-60	>60			Brain	Spine
Unobtainable MEP (*n*=11)	5	4	2	1	1	2	9
Unstable MEP (*n*=6)	2	4	0	1	1	2	4
Stable MEP (*n*=27)	5	22	0	1	2	8	19

NMB=Neuromuscular blocker during maintenance anesthesia, MEP=Motor evoked potential who were in the age group of more than 12 years, but the difference was not statistically significant.

Nearly, 76.5% of the cases (13 out of 17 cases) who showed unobtainable and unstable MEP outcome had lesion location in the spine as compared with 23.5% (4 out of 17 cases) that had lesion location in brain [Figure 2 and Table 3]. This difference was significant as demonstrated by the Chi-square test. On sub-analysis, poor MEP outcome in 4 of the 13 scoliosis cases and 8 out of the 19 cases operated for spine deformity were not found to be of statistical significance. The Stagnara wake-up test was employed in the case of an 11-year-old girl who presented with neurofibromatosis and progressive dorsolumbar scoliosis. She had prior surgery in the form of posterior fusion for scoliosis correction at the age of 10 years. The post-operative imaging revealed dextroscoliosis of the dorsal spine, Cobb's angle 84° (rigid), D9 hemivertebra and left lateral wedging. She did not have any pre-operative neurological deficits and her baseline SSEPs from all four limbs was normal. MEP responses were unobtainable even before incision. As per protocol, the MEP stimuli were delivered at regular intervals, but responses were lacking at all times. A Stagnara wake-up test was used after instrumentation with negative results. Recovery was uneventful. SSEP responses were well-preserved throughout the surgery.

Out of the 44 monitored patients three had a pre-operative deficit and 4 out of 44 cases received muscle relaxant during the maintenance anesthesia. However, no significant increase in the incidence of poor MEP monitoring outcome was noted in these two populations.

Reversible loss of MEP was encountered in 2 out of the 33 cases where MEPs were present and stable during the recording.

Case 1 was 32-year-old male doctor who presented with subacute onset mild right hemispheric weakness. He also had a history of recent onset seizures and was being treated with antiepileptic drugs. The only abnormalities on pre-operative examination were mild weakness and slightly increased tone in the right upper and right lower limb and extensor plantar response on the right side. His brain magnetic resonance imaging (MRI) showed a left paracentral tumor, a World Health Organization (WHO) Grade IV glioblastoma multiforme on subsequent histology. Pre-operative right median and right tibial SSEPs were normal. MEP recordings were well elicitable at baseline after anesthesia and after dural exposure. During the course of the surgery, serial stimulation revealed that MEP responses were unobtainable abruptly. At the time of loss of MEP, the surgeon confirmed close proximity to the motor strip and readjustment of retractors reversed the loss of MEPs [Figure 3]. The MEPs post-correction were robust and comparable with the baseline recordings. Though the patient had a history of seizures, transcranial stimulation for MEP was uneventful. No new post-operative deficit was noted and the post-operative neurologic status was unchanged from the pre-operative status.

Table 3: Association between lesion location and MEP outcomes

MEP outcome	Lesion location			
	Brain		Spine	
	No.	Percentage	No.	Percentage
Unobtainable (*N*=11)	2	18.2	9	81.8
Unstable (*N*=6)	2	33.3	4	66.7
Stable (*N*=27)	8	29.6	19	70.4

MEP=Motor evoked potential, By ^{2} test X1=9.53, *P*=0.0020, significant

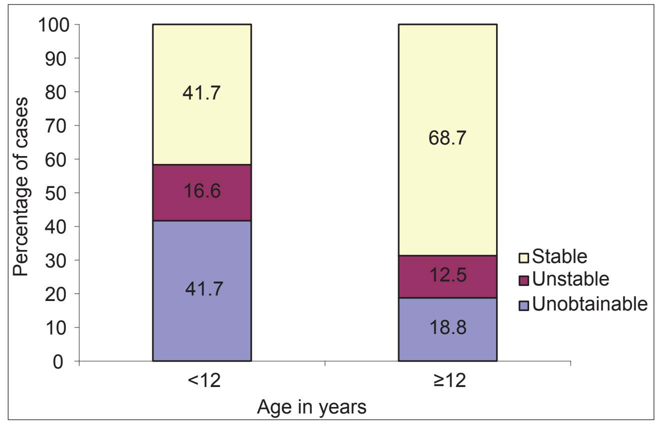

Figure 1: Association between age and motor evoked potential outcomes

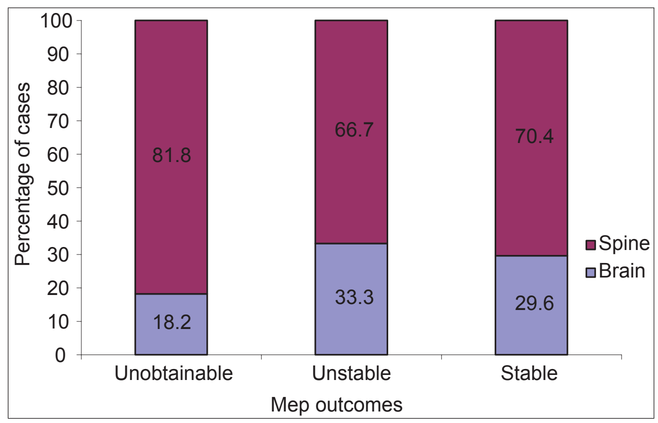

Figure 2: Association between lesion location and motor evoked potential outcomes At baseline Loss of MEP Return of MEP following during resection corrective measures

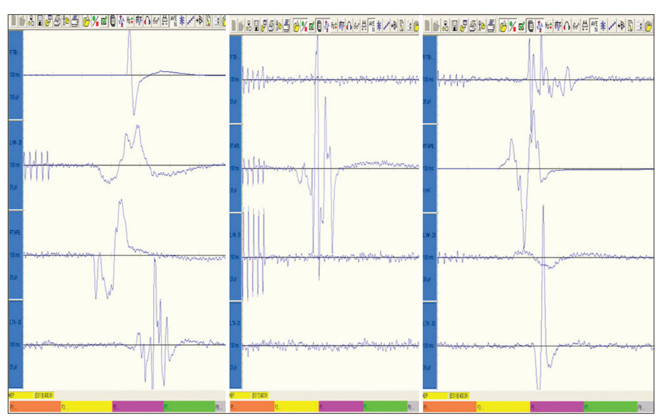

Figure 3: Transcranial motor evoked potential recording in a 32-year-old male with left paracentral glioma. In each box - first tracing-right tibialis anterior; second tracing-right abductor pollicis brevis, third tracing-left vastus medialis; fourth tracing-left tibialis anterior time base - 100 ms; amplitude calibration - 35 uv/div stimulus intensity - 400 V

Case 2 was a 48-year-old neurologically normal male who presented with paresthesia in his legs. MRI of the cervical spine revealed an intramedullary tumor at C5-6 level. His pre-operative SSEPs were normal from both median and both tibial nerves. MEP data was stable at baseline and following spine exposure. However, during a critical surgical stage, MEP data was lost. On alerting the surgeon, he reduced the degree of traction as the corrective maneuver. The MEPs returned and persisted throughout the surgery thereafter. No new post-operative deficit was noted. Histopathology showed a tanycytic ependymoma WHO Grade II.

Discussion

The Stagnara wake-up test has well-documented risks to patient such as extubation, possible loss of intravenous lines and recall. However, of prime importance is the fact that it does not indicate the time of onset of neurologic injury. On the other hand, the main advantage of MEP monitoring is that it allows nearly continuous monitoring of the corticospinal pathway during "high-risk" surgery. However, it has not been very widely used due to reservations about feasibility, safety and low success rates.

In this study, MEP monitoring was successfully obtained from the lower limbs in 75% cases. Xi Chen *et al*.[5] reported a success rate of 66% for lower limb MEP monitoring. A much higher success rate of 94% had been reported by Calancie *et al*.[10] which could be attributed in part to the careful patient selection involving exclusion of patients with significant pre-operative deficits.

There were technical limitations in this study. One of the technical factors contributing to poor MEP recording in some of the cases in the present study was high impedance probably due to electrode dislodgement during surgery. Furthermore, in some of the cases carried out at the start of this study, MEPs were recorded at the same intensity throughout from the start of surgery. Recording at higher intensity could have been attempted in these cases. These factors were ruled out subsequently among the technical variables as a contributing factor to poor MEP recording outcome. As a part of systematic troubleshooting, reversal of stimulus polarity was also carried out whenever needed. One should also keep in mind that there are local factors producing regional ischemia without altering the systemic blood pressure, which are known to contribute to loss of MEP recording.[11]

The incidence of poor MEP outcome was statistically significantly higher in the spine surgery group in this study (P = 0.0020). Thirteen out of the 32 patients operated for spine lesions had a poor MEP monitoring outcome. These 13 spine surgery patients were among the 17 out of the total of 44 patients of failed or poor MEP recording in this series. Further analyses showed that 8 out of these 13 patients had neuromuscular spine deformities. Four patients had dorsolumbar scoliosis, three had spina bifida and one was a case of atlantoaxial dislocation. A similar trend of difficult MEP recording and no recordable data in neuromuscular spine deformity surgeries has been observed in previous studies.[5,12-15] However, all patients in this series underwent MEP recording as a part of multimodality monitoring. In all cases with failed or unstable MEP recording, the other monitoring modalities were well-preserved throughout surgery.

Various criteria have been described in the literature for MEP monitoring during spine surgery. These include the complete disappearance of MEP - "presence or absence" method, "threshold criterion" based on an increase in the threshold of stimulus intensity by 100 mV, "amplitude" criterion based on a 50%-80% decrease in the amplitude of the MEP response and "waveform" criterion based on the changes in the morphology (polyphasic to biphasic to loss of waveform) of the MEP waveform.[5,8,10,16,17] All methods have been reported to be successful during spine surgery. The criterion of a 100 mV increase in the threshold of stimulation described by Calancie is specific to a particular type of stimulator (digitimer D185) and requires manual delivery of stimulus when higher voltage is needed in case of smaller MEP responses, thereby making it technically complex. Moreover, to use this criterion on other stimulators, initial calibration would be needed to define the criteria.

The potential problem in the amplitude-based and morphology-based criteria is the trial to trial variability of MEP responses making it difficult to establish an initial baseline and also to make subsequent comparisons. Furthermore, immediately after induction higher stimulus intensity is required to elicit MEP responses, which can be attributed to the confounding effect of anesthesia. In patients with pre-operative neurological deficit, the stimulus parameters would vary in the affected and unaffected muscle groups. These factors would vitiate all the three types of criteria; viz-threshold-based, amplitude-based and morphology-based methods because a down trend is noted in the stimulus intensity during the course of the surgery, which would alter the responses in terms of criteria from baseline. Since there are several variables that can interfere with the MEP recording during the course of surgery such as detached electrodes, hypothermia, hypotension, effects of anesthesia; in this series the simple "presence or absence" method was used.[4,5] This means that if following transcranial stimulation, the MEP responses were present in the "target muscles" (which were distal to the lesion) then the situation did not warrant an alarm. It the responses disappeared then the surgical team had to be warned.

Epilepsy may provoke seizures related to transcranial stimulation.[18] Out of the 12 patients who underwent MEP monitoring for brain surgery in this series 6 patients had seizures pre-operatively. No case of intraoperative seizure was encountered. Very brief high frequency pulses used during MEP stimulation appear to have a very low, but not negligible association with seizures.[19]

The incidence of false negative MEP recording i.e. - new deficit despite full recovery of MEP or persistently stable MEP has been reported at 0.03-0.06%.[20] This has been attributed to use of excessively high current leading to elicitation of MEP caudal to the target territory and the lesion remaining unnoticed or occurrence of deficits in unmapped muscle groups.[21,22] Though the number of patients in this series is small, there were no new post-operative deficits. Furthermore, the use of dense muscle recording from several muscle groups and the use of multimodality intraoperative monitoring helped to minimize to the incidence of false negatives in our institution.[23]

Finally, detailed analysis to enable the assessment of a significant statistical association between poor MEP monitoring outcome and factors such as extremes of age, surgery for spine deformity, presence of pre-operative deficit and use of muscle relaxant during maintenance anesthesia was limited in this study by the small sample size. A future study is planned in our institution with a larger number of patients so as to allow better statistical analysis.

Conclusion

This series showed that MEP monitoring can be employed safely in "high-risk" brain and spine surgeries with reasonable success by using dense coverage for MEP recording and detailed attention to technical factors. Certain situations viz-extremes of age and spine surgeries for deformities have a predilection for poor MEP monitoring outcome. Apart from a dense recording protocol, other measures like multimodality monitoring should be considered in these special situations to enhance the sensitivity of MEP monitoring outcome.

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