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Intramedullary Spinal Cord Tumor Surgery: The Utility of Multimodal Intraoperative Neurophysiologic Monitoring

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ABSTRACT

Intramedullary spinal cord tumors (IMSCT) account for about 2-4% of tumors of the central nervous system. Surgical resection continues to be the most effective treatment modality for the majority of intramedullary tumors with gross total resection leading to preserve neurologic function and improved survival. However, surgical treatment is often difficult and carries significant risk of postoperative neurologic complications.

Intraoperative neuromonitoring has been shown to be of clinical importance in the surgical resection of IMSCT. The main monitoring modalities include somatosensory-evoked potentials (SSEP), transcranial motor-evoked potentials (TcMEP) via limb muscles or spinal epidural space (D waves) and dorsal column mapping. These monitoring modalities have been shown to inform surgeons intraoperatively and in many cases, have led to alterations in operative decision. Herein, we reviewed the literature on the utility of intraoperative neuromonitoring for intramedullary spinal tumor resection and its role in predicting post-operative neurologic deficits. Medline search was performed (2000-2015) and thirteen studies were reviewed. Data was extracted depicting the role of monitoring in outcomes of surgery. By utilizing intraoperative SSEP, TcMEP, D-waves and dorsal column mapping, spinal injury could be prevented in majority of cases, thereby improving post-operative neurologic functioning and outcome in patients undergoing surgery for IMSCT.

KEY WORDS: Intramedullary tumor, intraoperative monitoring, outcomes, spinal injury

INTRODUCTION

Intramedullary spinal cord tumors (IMSCT) account for about 2-4% of tumors of the central nervous system and about 15% of adult intradural tumors (2,7,9,20,40). The most common IMSCT include ependymomas and astrocytomas. Unlike most brain tumors, these are often benign and have an insidious onset with presenting symptoms including paresthesia, weakness, spasticity, gait instability, and bowel/bladder dysfunction. Surgical resection continues to be the most effective treatment modality for the majority of intramedullary tumors with gross total resection leading to preserve neurologic function and improved survival (7,15,19). However, surgical treatment is often difficult and carries significant risk of postoperative neurologic complications. Studies have reported deterioration in neurologic function in patients postoperatively (9,25,59) with rates of dorsal column dysfunction as high as 43.6% to 55.1% (9,38,57). These deficits severely affect the postoperative functionality of patients as they are often left with significant morbidity worse than their preoperative disease burden (52,66,67). Part of the surgical difficulty stems from the inability to identify the appropriate resection plane to delineate the extent of resection. Also, the presence of tumor can distort the normal anatomic architecture of the spinal cord, making it difficult to ascertain the physiologic midline for a myelotomy. As a result of these surgical challenges, intraoperative neuromonitoring has gained favorable grounds in facilitating maximal tumor resection while minimizing neurological morbidity (31,46,47,56).

Intraoperative neuromonitoring has been shown to be of clinical importance in the surgical resection of intramedullary spinal cord tumors (8,11,30,39,54,56,61). The main monitoring modalities include somatosensory evoked potentials (SSEP), transcranial motor evoked potentials (TcMEP) via limb muscles or spinal epidural space (D waves) and dorsal column mapping. SSEPs provide information about the functionality of sensory pathways. Despite earlier studies showing reduction of quadriplegia from 3.7% to 0% (16) and from 6.8% to 0.7% (43) using intraoperative SSEP monitoring, post-operative motor deficits were being reported regardless of the unchanged intraoperative SSEP (27,33,34,70). As a result, transcranial MEP has been used as a direct method of monitoring motor pathways during surgery for intramedullary spinal tumor and other spinal pathologies (12,22,35). Consequently, the combined utilization of SSEP and MEP provides increased accuracy in detecting injury to sensory and motor pathways that can be affected differently depending on the location and morphology of the tumor (23,50). Dorsal column mapping using micro-stimulation and SSEP recording is another modality being utilized to determine anatomic landmarks such as dorsal median sulcus to guide midline myelotomy. These monitoring modalities have been shown to inform surgeons intraoperatively and in many cases, have led to alterations in operative decision. Herein, we reviewed the literature on the utility of intraoperative neuromonitoring for intramedullary spinal tumor resection and its role in predicting post-operative neurologic deficits.

MATERIALS AND METHODS

The MEDLINE database was queried using the following search items: "Intramedullary tumor", "spine", "spinal tumor", "monitoring", "neuromonitoring", "somatosensory evoked potential", "motor evoked potential" and "dorsal column mapping". Only articles in English language, and published between 2000 and 2015 were considered. Publications excluded from our search were Non-English language articles, abstract-only publications or articles not available via our electronic database queries. Individual case reports were also excluded. Manuscripts were identified and reviewed. Detailed information and data from the selected manuscripts were assessed and compiled.

RESULTS

After extensive search for available manuscripts, 13 studies were selected for inclusion in this review. Table 1 shows a summary of the relevant clinical studies and the intraoperative monitoring modalities and post-operative changes in neurologic status. One of the articles (study 1) was a historical control study whereby patients who underwent surgery for intramedullary spinal tumor with intraoperative monitoring were matched and compared with previously operated patients without monitoring. Two of the articles (studies 5 and 6) were prospective while the remaining 10 studies were retrospective chart reviews. Full review was performed in all 13 articles. These were all clinical studies whereby intraoperative neurophysiologic monitoring was utilized for the surgical resection of intramedullary spinal cord tumors. The number of patients ranged from a minimum of 12 (study 11) to a maximum of 203 (study 5). Among the patients in each study, intraoperative monitoring was successful in 12% of patients in study 2 and 100% of patients in studies 7, 8, 11-13. MEP, SSEPs and D-waves were also recorded in most of the studies. One study utilized dorsal column mapping (study 2).

Two studies reported the sensitivity and specificity in predicting post-operative sensory deficits using SSEP only. In study 7, sensitivity and specificity were 75% and 50% respectively for SSEP while in study 12, sensitivity and specificity were 80% and 100% respectively for SSEP only. TcMEP was more commonly reported. When the all-or-none criterion was used, the sensitivity / specificity of muscle or myogenic TcMEP only was reported as 95% / 98.1% in study 5 and 53% / 93% in study 13. When the criterion for a significant TcMEP was defined as greater than 70% deterioration in signal amplitude, the sensitivity increased from 53% (all-or-none criterion) to 79% while the specificity dropped from 93% (all-or-none criterion) to 49% in study 13. In utilizing the combined approach of motor and sensory monitoring, study 7 showed an increase in sensitivity from 100% in MEP only and 75% in SSEP only to 100% in the combined approach. However, in the same study, there was a difference in specificity from 25% in MEP only and 50% in SSEP only to 28.5% in the combined approach. Similarly in study 13, there was an increase in sensitivity from 80% in SEP and 75% in MEP to 100% in the combined approach while the specificity dropped from 100% in both SEP and MEP to 83.3% when both approaches were combined.

Intraoperative neuromonitoring (IONM) accurately predicted postoperative outcome in all of the studies included. Sala et al (56) illustrated that patients with

Table 1: Summary of clinical studies utilizing intraoperative neurophysiologic monitoring during surgical resection of spinal intramedullary tumors

Study	Type	Total no. Pts	No. pts with IONM	IMST / EMST	Modality of interest	Surgical Intervention	Study conclusions / post-op outcome
1. Sala et al (2006)	H/C	100	50	100 IMST	mMEP and D-waves	Surgical field adjustment; warm irrigation, correct hypotension; abort surgery if loss of D-waves	Better improvement in McCormick grade at 3 months in the IONM group (mean, +0.28) vs. Historical Control group (mean, -0.54), p=0.0016
2. Mehta et al (2012)	R	91	11	91 IMST	DCM and SSEP	-	Dorsal column dysfunction = 9% in patients with DCM and 50% in patients without DCM (p=0.01)
3. Quinones et al (2005)	R	28	27	28 IMST	MEP and SSEP	-	Loss of TcMEP waveform in 12 pts correlated with worse motor deficits compared to pts without loss of waveform (p<0.0001)
4. Jin et al (2015)	R	30	25	30 IMST	mMEP and SSEP	-	1mth post-op, all/none SEP-mMEP with fEMG. Sensitivity/Specificity=100% / 91%. PPV/NPV=60% / 100% fEMG accurately predicted upcoming MEP events
5. Forster et al (2012)	P	203	47	50 IMST	MEP and SSEP	Resection halted; Blood pressure elevated; operative modifications	MEP (all or none): Sensitivity=95.0%; Specificity=98.1% in detecting motor deficits SSEP: Sensitivity=94.4%; Specificity=96.8% in detecting sensory deficits
6. Rajshekhar et al (2011)	P	110	75	44 IMST	mMEP	-	Post-op worsening in 8% of pts with MEP recording vs. 17.1% in pts without MEP (p=0.052)
7. Hyun et al (2009)	R	19	19	19 IMST	mMEP and SSEP	Temporary halt; correct hypotension; change strategy to piecemeal resection; warm irrigation; Steroids	MEP: Sensitivity=100%; Specificity=25% SSEP: Sensitivity=75%; Specificity=50% Combined MEP/ SSEP: Sensitivity=100%; Specificity=28.5%
8. Ando et al (2015)	R	13	13	13 IMST	Sp-SCEP and Br-SCEP	Temporarily halt	Combined Br/Sp-SCEP Sensitivity & PPV=66.7%; Specificity & NPV=90%

Table 1: Cont.

Study	Type	Total no. Pts	No. pts with IONM	IMST / EMST	Modality of interest	Surgical Intervention	Study conclusions / post-op outcome
9. Choi et al (2014)	R	76	50	76 IMST	mMEP and SSEP	-	GTR rate was 76% in IONM group versus 58% in non-IONM group (p=0.049)
10. Costa et al (2013	R	101	97	23 IMST	mMEP, D-waves and SSEP	-	Presence of persistent stable D-waves (n=13) predicted good motor outcome despite deterioration/loss in m-MEPs
11. Cheng et al (2014)	R	12	12	12 IMST	mMEP and SSEP	Temporary halt; release traction;	TcMEP Sensitivity=80%; Specificity=71.4%; PPV=66.7%; NPV=83.3%
12. Skinner et al (2005)	R	13	13	13 IMST	mMEP and SSEP	Wake-up test; temporary halt; Increase BP; Abort surgery;	fEMG abnormality leads to anticipation of MEP loss and predicts post-op motor deficits SEP: Sensitivity=80%; Specificity=100%; TcMEP: Sensitivity=75%; Specificity=100%; Combined SEP/MEP: Sensitivity=100%; Specificity=83.3%; fEMG: Sensitivity=87.5%; Specificity=83.33%
13. Muramoto et al (2014)	R	13	13	13 IMST	mMEP	Temporary halt; warm irrigation; increase BP; abort surgery with steroid administration	MEP (all or non criterion): Sensitivity=53%; Specificity=93%; MEP (<70% criterion): Sensitivity=79%, Specificity=49%

IONM=Intraoperative neuromonitoring; **IMST**=Intramedullary Spinal Tumor; **EMST**=Extramedullary Spinal Tumor; **mMEP**=Muscle Motor Evoked Potential; **DCM**=Dorsal Column Mapping; **Sp-SCEP**=Spinal Cord Evoked Potentials; **Br-SCEP**=Brain Evoked Potentials; **GTR**=Gross total resection; **fEMG**=free-running EMG; **H/C**=Historical Control; **R**=Retrospective; **P**=Prospective.

IOM had a better improvement in McCormick grade at 3 months compared to the historical control group without monitoring (p=0.0016). Also, Mehta et al (41) showed a 41% relative decrease in the rate of dorsal column dysfunction. In most of the studies, patients with significant changes in intraoperative monitoring had worse neurologic outcomes postoperative.

DISCUSSION

Surgical resection for intramedullary spinal tumors remains a challenging operative dilemma whereby the extent of resection is often sacrificed for impending neurologic damage. Studies have reported transient and permanent neurologic impairment following resection of these tumors (15,70). Fortunately, with the steady rise in microsurgical techniques, diagnostic imaging and intraoperative monitoring modalities, there has been a decline in postoperative neurologic morbidities in patients undergoing surgery for intramedullary spinal tumors (8,11,30,31,39,54,56,61). This has allowed for a more aggressive approach towards resection, aiming at maximizing resection and minimizing neurologic deficits (7,24,60,65). Neurophysiologic monitoring, not only guides the extent of resection, but serves as a predictor of neurologic outcomes and in many cases, provides critical information to the surgeon intraoperatively to alter surgical approach and avoid spinal injury. We reviewed 13 studies and overall, changes in SSEP, TcMEP and D-waves correlated with post-operative neurologic outcomes.

Somatosensory evoked potential:

SSEP monitors sensory pathways in the posterior column of the spinal cord. For SSEP monitoring, surface stimulating electrodes are mostly placed in bilateral extremities, usually the median nerve at the wrist and posterior tibial nerve at the ankle. The posterior tibial nerve, at the medial malleolus, is easily accessible for intraoperative stimulation and provides reliable data (48). Monitoring of nerves in the upper and lower extremities allows for comparison and changes may indicate anesthesia related effects or pre-operative positioning effect as seen in brachial plexus injury (32). Electrical stimulation of varying frequency, amplitude and duration is applied to the surface electrodes on the nerves. These signals are then acquired using continuous averaging of hundreds of consecutive sweeps of electrical stimulation over several minutes and are repeatedly compared to initial baseline recordings normally made after incision. SSEP is then recorded from scalp electrodes which provides cortical and subcortical data regarding the sensory pathways (42). Due to the averaging of this SSEP signal, the amplitude and latency recordings from the scalp electrodes will always lag behind real-time physiologic constraints by approximately 5-20 minutes (58). Intraoperative changes in the amplitude of SSEP of greater 50% and increase in latency of 10% compared to baseline values are considered abnormal (10).

Transcranial motor evoked potential:

TcMEP provides data on the descending corticospinal tracks by stimulation at the level of the cerebral cortex. Transcranial stimulation of the motor cortex is achieved via scalp electrodes. Stimulation can be magnetic through coils placed over the cortex (18) or electrical stimulus via subdermal electrodes (3). Peripheral data for TcMEP recordings can be obtained either from the end muscle via electromyography or from the spinal cord via D-waves. Common muscles monitored include the tibialis anterior and abductor hallucis in the lower extremities and the abductor pollicis and extensor digitorium of the upper extremities (6,11,54,63).

D-waves indicate corticospinal action potentials initiated by activation of fast axonal fibers with velocity of approximately 50m/s (36,49). This conduction speed of the fast fibers makes it possible to monitor motor pathways in real time without any delays as seen in SSEP. Monitoring of D-waves is achieved by electrodes placed in the spinal epidural or subdural space, rostral and caudal to the tumor being resected (25,29,44). The rostral electrode serves as the control since is detect signals from the cortex before being transmitted through the distorted tumor environment. Recordings from the caudal electrode is then compared with the rostral, and changes in peak-to-peak amplitude of D-waves by 50% or increase in latency by 10% was considered abnormal by most studies (17,45,54). Some advantages of D-waves include less sensitivity to halogenated anesthetics, which could interfere with signal recordings in SSEP and muscle TcMEP (62). Additionally, neuromuscular blocking agents commonly used during surgical procedures do not affect D-wave recordings (37). Also, since D-waves only monitor the fast motor fibers, they are more sensitive in detecting early injury to the spine.

Myogenic TcMEP recordings from extremity electrodes are derived from the same transcranial electrical stimulation as D-waves. They indicate compound muscle action potentials and like D-waves, are real time and do not require averaging. There are certain advantages of the muscle MEP over the D-waves. When measuring signals from the muscles, not only does this reflect functionality of the entire motor system, it helps delineate laterality. Given that D-waves only monitor corticospinal tract axons, recordings will not be quite reliable below the level of T12 and as such, conus tumors cannot be monitored with D-waves. Recordings from muscle electrodes make it possible to monitor lowest sacral roots including sphincter muscles. In order to determine which change in recorded signal from muscles is considered significant, some studies have used the all-or-nothing approach as a criterion for significant signal change intraoperatively (13,33). Meanwhile some studies have utilized greater 50% or 70% decrease in signal amplitude from initial baseline to indicate significant change (23,26,45,56).

Dorsal column mapping:

This is mainly performed to identify anatomic landmarks such as dorsal median sulcus to guide a safe midline myelotomy. This is very useful in cases where the tumor has distorted the normal spinal anatomy. Here, needle electrodes are placed in the lower extremities to capture data from peripheral nerves (e.g posterior tibial nerve at the medial malleolus). Micro-stimulation is applied around the margins of the tumor using a hand-help bipolar electrode. The bipolar tip is placed on the dorsal aspect of the cord and stimulation is applied form lateral to medial. The physiologic midline is the region where there is complete absence of a response or the point of lowest relative amplitude in the sweep from lateral to medial. SSEP recordings acquired during the stimulation help determine the myelotomy site, identify the resection plane and guide extent of resection (4,41).

This review highlights the critical role of intraoperative neurophysiologic monitoring during resection of intramedullary spinal tumors and how recorded data can affect management and predict neurologic outcomes. Sala et al (56) demonstrated the importance of applied motor evoked potentials on post-operative neurologic outcomes using a historical control study. The study evaluated 100 patients who underwent surgery for intramedullary spinal tumor and compared the outcomes of patients who had intraoperative monitoring with D-waves or muscle MEP to those without monitoring. They observed a significantly greater improvement in functional outcomes using the McCormick grade at 3 months postoperative in the patients that had intraoperative monitoring (mean, +0.28) compared to the historical cohort without monitoring (mean, -0.54), p=0.0016. Another study of 110 patients with spinal tumors (44: intramedullary; 66: extramedullary) showed significantly better motor outcomes in patients with successful intraoperative monitoring during discharge from the hospital (53). In this study, post-operative worsening of motor deficits was present in 8% of patients with TcMEP recording compared to 17.1% in patients without monitoring (p=0.052). Despite these studies demonstrating the crucial role of IOM, false negatives have been reported especially when utilizing SSEPs only as patients present with post-operative motor deficits. These isolated motor pathway related injuries are not merely flaws of the SSEP monitoring modality, but rather represent injuries outside the monitoring capability of SSEP. As such, combined modalities are increasingly being utilized to provide a broader coverage in avoiding neurologic injury.

Several studies have shown that no single modality sufficiently monitors all pathways in the spinal cord (11,14) with the goal of avoiding injury to both sensory and motor pathways (48). By directly manipulating the spinal tracts during resection of intramedullary tumors, there is a high risk of injury to motor and sensory tracts. To circumvent the delayed acquisition in SSEP recordings due signal averaging, the addition of transcranial MEP allows for real-time monitoring and feedback, thereby enabling surgeons to engage in immediate corrective actions before an injury to the spine becomes irreversible. With sensitivity and specificity of 100% and 83.3%, Skinner et al (61) effectively illustrated the role of the combined utilization of SSEP and TcMEP.

Studies have reported that with less than 50% change in D-wave amplitude even with complete loss of TcMEP from muscle electrodes, there is only transient paraplegia, with most patients achieving full recovery within hours to weeks postoperative (28,31,56). Meanwhile, intraoperative loss of D waves results in permanent paraplegia postoperative (56). Changes in D-wave amplitude / latency directly signify change in signal transduction of the fast action fibers in the corticospinal tract rather than in the muscle, thereby providing a better predictive value of post-operative outcome. It should also be mentioned that the all-or-nothing approach to TcMEP monitoring presents inherent dangers to the spinal cord during tumor resection. A study by Skinner et al (61) showed that abnormality in free-running EMG leads to anticipation of TcMEP deterioration and predicted post-operative motor deficits with a sensitivity of 87.5% and specificity of 83.3%. As such, awaiting a complete loss of TcMEP to alter surgical decision can be detrimental to the patient.

Dorsal column mapping can also provide additional surgical benefit. A study by Mehta et al (41) of 91 patients undergoing surgery for intramedullary tumor showed a significant decrease in rate of postoperative dorsal column dysfunction from 9% in patients with intraoperative dorsal column mapping to 50% in patients without mapping. Mapping facilitates localization of the anatomic midline, identification of operative tumor/spinal cord plane and guide the extent of resection with the goal of maximum tumor resection with minimal neurologic morbidity.

The combined monitoring approach allows the surgeons to sample a broader range of the spinal tracts to detect injury with sensitivity and specificity as high as 100% and 91% as reported by Jin et al (26). This combined modality facilitates the avoidance of spinal cord injury with intraoperative changes serving as a good predictor of post-operative functional deficits. Choi et al (6) demonstrated that when a combined monitoring approach is utilized, gross total resection can be achieved in about 76% of patients with monitoring versus 58% in patients without monitoring (p=0.049), thereby outlining the strength of the combined modality.

Intraoperative Intervention When Signal Deteriorates:

One critical role of intraoperative monitoring is the effect on operative decisions. Once changes in recorded amplitude of SSEP, muscle MEP or D-waves are deemed significantly worse, a decision has to be made by the surgeon whether to abort the procedure, change surgical approach, or execute other intraoperative measures and later resume tumor resection. In the immediate period following a loss in MEP or deteriorating SSEP during resection of intramedullary tumors of the spine, three key factors have been identified to promote signal recovery and improve outcome: Time, Irrigation and Blood Pressure (11,23,55,68,69). By temporarily halting the surgical resection with continuous monitoring of neurophysiologic parameters, surgeons can obtain real time data as to the degree of injury to the spinal cord and if further manipulations are possible (11). Despite the paucity of data on the exact wait time, the general trend was to immediately suspend the surgical resection and release retractors while continuing SSEP and TcMEP monitoring until signals return to below critical levels. Sala et al (54) reported transiently stopping surgery for about 30 minutes or more in order to allow signals from TcMEP and D-waves to return to below critical levels before further manipulating the cord. Recovery of signal often leads to continuation of the tumor resection. Continuous deterioration of signal or complete loss for an extended period may lead to aborting the procedure entirely. Therefore, a transient halt in tumor resection and releasing retraction from the surgical bed could perhaps be the most critical variable in affecting recovery and postoperative outcome. The second factor is irrigation of the surgical field with warm saline solution, which dilutes accumulated potassium in the extracellular matrix, thereby preventing blockage of nerve impulse transmission. Furthermore, irrigation clears out residual blood products and cellular metabolites (68,69). The third factor is increasing mean arterial blood pressure to enhance local perfusion of the spinal cord and prevent ischemia. Several studies have reported favorable neurologic outcomes when mean arterial blood pressure was increased in the event of decreasing intraoperative monitoring signals (23,48,51,61). Hyun et al (23) elevated MAP to 91mmHg to facilitate increased blood flow to the spinal cord. Another study by Choi et al (6) demonstrated that elevating the MABP to at least above 60mmHg facilitated recovery. These intraoperative measures are often used in combination and are targeted towards recovery of spinal cord signal, minimizing neurologic injury in order to resume maximum possible resection of the intramedullary tumor.

Another measure to decrease spinal cord injury is the administration of steroids preoperatively. All the patients in Mehta et al (41) were administered steroids prior to surgical resection. High dose intravenous corticosteroids may potentially improve transient neurologic function by reducing inflammation and vasogenic edema around the tumor, thereby relieving the spinal cord from the compressive effects of the tumor. Experimental studies on laboratory animals have demonstrated that early delivery of methylprednisolone following acute traumatic spinal cord injury can be beneficial, with larger animals having more favorable outcomes (1,5,21,64). However, the role of steroids following spinal cord injury in humans is still highly controversial. Pre-operative steroid administration is a common therapeutic adjunct in patients undergoing surgery for intramedullary spinal tumor. In two studies (study 3 and 7), corticosteroid was administered intraoperatively once surgery was stopped due to loss of TcMEP from multiple muscles.

CONCLUSION

Intraoperative neuromonitoring using a combination of dorsal column mapping, SSEP, muscle TcMEP and D-waves provides surgeons with anatomic landmarks for midline myelotomy, indications of the resection plane and guidance to the extent of maximum tumor resection with minimal neurologic morbidity. Studies continue to demonstrate favorable postoperative outcomes when these monitoring modalities are used in combination. Reports of intraoperative factors such as time, irrigation and blood pressure to facilitate recovery from a lost intraoperative signal remain promising as means of mitigating neurologic injury. However, larger, multi-center, randomized controlled studies are needed to determine standardized treatment protocols in the event of a loss in intraoperative SSEP or TcMEP during surgery for spinal intramedullary tumor.

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