RETROSPECTIVE ANALYSIS

The influence of anesthesia on intraoperative neurophysiological monitoring during spinal surgeries

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ABSTRACT

BACKGROUND: Intraoperative neuromonitoring using tc-MEPs satisfactorily detects motor tract integrity changes during spinal surgery. However, tc-MEP is affected by anesthesia and other factors, in which the stimulation threshold increases because the waveform amplitude decreases over time with the accumulation and boluses of anesthetics.

METHODS: We conducted a retrospective study of 139 patients. The average age was 30 years. Tc-MEPs were recorded bilaterally from the tibialis anterior muscle and the abductor hallucis muscle. Statistical tests were used to investigate the changes to evaluate anesthetic effects.

RESULTS: There were no significant differences in tc-MEP amplitude change (%) between the groups of propofol (13 %), remifentanil (22 %) and sufentanil (26 %, p < 0.01). Significant differences were found between the groups of propofol, remifentanil, and sufentanil (20 %) and bolus sufentanil (–30 %), and bolus ketamine (730 %, p < 0.008). Major differences were observed between bolus sufentanil (–30 %) and bolus ketamine (730 %, p < 0.001). When comparing tc-MEPs with no amplitude, no significant difference was found between the groups of propofol (26 %), remifentanil (24 %), and sufentanil (28 %, p < 0.007). Substantial difference was found between the groups of propofol, remifentanil, and sufentanil (mean 26 %) and the group where ketamine boluses were administered. We didn't observe any loss of amplitude (0 %, p < 0.0002).

CONCLUSION: IONM may be useless in patients where boluses of sufentanil are administered and also with Medical Research Council grades 3 and below. Consider applying IONM in patients with severe spinal deformity along with a higher age of over 50 and neurological deficit. Increasing stimulus intensity or facilitation techniques may be considered to improve the usefulness of tc-MEP. Our concept of findings supports the neurophysiological monitoring findings in other studies *(Tab. 10, Ref. 45)*. Text in PDF *www.elis.sk*.

KEY WORDS: neuromonitoring, MEP, motor evoked potential, spinal deformity, anesthesia, propofol, sufentanil, ketamine, amplitude.

Introduction

Spinal surgery with intraoperative neurophysiological monitoring (IONM) is advancing and becoming prevalent (1–3). Transcranial motor evoked potentials (tc-MEPs) are universally recorded during intraoperative monitoring to ensure the integrity of the descending spinal cord, but indications in lower risk decompressive surgeries are more controversial (4). The integrity of the spinal cord is the main assessment of electrophysiologic monitoring together with the entire team participating in the operation of the spine to recognize and avoid injury to the spinal cord (5). Despite all this, tc-MEPs have excellent sensitivity for detecting changes in motor tract integrity during spinal surgery (6–8). In general, patients with scoliosis are neurologically intact, compared to those who are undergoing surgery for intramedullary or extramedullary spinal cord disorders. MEPs are susceptible to the effects of perioperative environmental factors. Amplitude in MEPs can decrease even in the absence of any nerve damage (false positive), caused by intraoperative hypotension, hypothermia or electrode failure (9, 10). Volatile anesthetic agents suppress the excitability of the motor cortex, resulting in diminished amplitudes (11, 12). To decrease inhalational anesthetic effects, it is recommended to apply total intravenous anesthesia (TIVA) instead of volatile anesthetics (11, 13). The intraoperative application of muscle relaxants solely following intubation has been suggested as the preferred anesthetic technique for surgeries with MEPs (14). It has been reported that anesthetic agents such as propofol suppress MEPs, while intravenous ketamine (ket) does not suppress MEPs and may even facilitate them (15–19). In a dose dependent fashion, in addition most anesthetics, other than remifentanil and ketamine, can cause false positive results by inhibiting MEPs (20). Optimal conditions and an adequate depth of anesthesia ensure TIVA using a propofol infusion along with stable blood pressure, core temperature and avoidance of excessive blood loss (21–23). Other published studies showed fading MEP with prolonged exposure to anesthesia

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described as "anesthetic fade" (5). In his study, MacDonald et al (24) found abrupt lower limb MEP loss during prolonged scoliosis surgery restored after instrumentation release without neurologic deficit and suggested increasing MEP stimulation parameters to offset this effect. There is limited information on whether a balanced technique of anesthesia improves increased IONM changes. There is also a paucity of information on the intraoperative anesthetic and surgical interventions performed on notification of an IONM change (25). Holdefer et al found no evidence of a reducing trend of amplitude over time (26). This has been confirmed by another study which also found no significant change of MEP amplitude over 120 min. during surgery of propofol anesthesia (27). Surgeons should understand the rationale and clinical basis for IONM to interpret the monitoring changes and to utilize them for a better surgical outcome.

The purpose of this study was to compare several different groups of patients, and how the type of spinal deformity and contingency of neurological status versus different types of anesthesia ultimately affect the tc-MEP waveforms.

Materials and methods

Approval of the study was obtained by the institution's ethics committee of University Hospital Bratislava, Slovakia (EK/62/2019). No patient consent was deemed necessary. All records and personal data of patients were anonymized.

Study design

We conducted a retrospective study of 139 patients between January 2007 and January 2018. All of these patients underwent corrective spinal surgery in our department together with IONM requiring tc-MEP indication as determined by the operating surgeon. Patients ranged in age from 12 to 79 years (standard deviation, mean 18). Regarding sex, there were 22 males and 117 females in the study. The inclusion criteria were all the patients that had a tc-MEP performed during spinal surgery. There were no exclusion criteria (Tab. 1).

Data source collection

The electronic and paper patient medical data were reviewed for all 139 patients. The data collected included general patient information (age, height, weight, sex, date of study) (Tab. 2), anesthesiology data (type, hemodynamics, physiological values), and surgical as well as neuromonitoring information (type of spinal deformity, procedure, monitoring techniques, events in tc-MEP change for each electrode separately, variables).

The types of spinal deformities were divided into six groups and a subgroup of neurological deficit alone (Tab. 3). The surgical procedure in the AIS2-4, neuromuscular and degenerative scoliosis groups was usually performed with dorsal transpedicular stabilization with correction of scoliosis. Severe scoliotic curves were treated with combined surgical procedures that consisted of osteotomies and lateral approaches. Other spinal deformities (I), usually degenerative, were treated with dorsal transpedicular stabilization along with laminectomy and spinal decompression. Complications and/or post-operative neurological outcomes were also collected in the neurological deficit (ND) subgroup. We used Medical Research Council (MRC) grading. Modification of the MRC grading was made as we added a sensory deficit (MRC 5 normal strength with sensory deficit) and radicular pain (MRC 6 normal strength with radicular pain).

Anesthetic management

In all patients, anesthesia was maintained with total intravenous anesthesia (TIVA) during the period of MEPs. A muscle relaxant, rocuronium bromide (Esmeron 30–50 mg), was administered before intubation. Perioperatively, after induction and intubation, all muscle relaxants were discontinued during surgery. An arterial line was placed to monitor blood pressure. Other standard monitoring, such as electrocardiogram and oxygen saturation was managed by the anesthesiologist.

The patients were classified into five groups: propofol; propofol with remifentanil; propofol with sufentanil; propofol with bolus sufentanil; propofol with ketamine bolus (Tab. 4). Propofol, sufentanil and remifentanil were administered as shown (Tab. 5). Sufentanil boluses were administered in doses of 3 ml intravenously (5 µg/ml). Ketamine boluses were administered in doses of 30 mg intravenously (50 mg/ml).

Tab. 1. Patient selection, inclusion and exclusion criteria.

Inclusion criteria
Patients who underwent a surgical procedure for spinal surgery with IONM of tc-MEP
Exclusion criteria
Depends on each group, subgroup

Tab. 2. Patient characteristics according to groups of spinal deformities and neurological deficit subgroup.

Groups of patients	number (n)	age (years)	weight (kg)	height (cm)	sex (M/F)	hgb (g/l)
Total	139	27	59	165	22/117	44.3↘
AIS2	64	17	54	166	4/60	45.4↘
AIS3	27	19	54	162	4/23	49.6↘
AIS4	3	16	51	163	0/3	42.7↘
N	8	19	50	162	2/6	52.0↘
D	16	55	66	164	2/14	37.3↘
I	21	51	77	170	10/11	38.8↘
Neurological deficit (ND)	43	48	62	162	10/33	42.2↘

Values are presented as a number. ↘ indicates a decrease of hgb during the entire anesthesia time.

Tab. 3. Groups of spinal deformities and neurological alteration subgroup.

Total – complete sample of all patients in all groups
AIS2 – adolescent idiopathic scoliosis grade II, (Cobb angle = 30° - 60°)
AIS3 – adolescent idiopathic scoliosis grade III, (Cobb angle = 60° - 90°)
AIS4 – adolescent idiopathic scoliosis grade IV, (Cobb angle > 90°)
D – degenerative scoliosis all grades,
N – neuromuscular scoliosis all grades,
I – other spinal deformities (metastases, spinal stenosis, herniated discs, other)
ND – neurological deficit (separate subgroup of patients with ND before or after spinal surgery)

Tab. 4. Patient characteristics in correlation with anesthetics.

Anesthetics	Number of patients (n)	Age mean (years)	Weight mean (kg)	Height mean (cm)	Sex No. of patients (M/F)	Hgb mean (g/l)
Total/Propofol	139 (100)	30	59	165	22(16)/117(84)	44↘ (34)
Remifentanil	75 (54)	29	60	166	10/(13)/65(87)	45↘ (34)
Sufentanil	64 (46)	25	57	166	12(19)/52(81)	44↘ (34)
Bolus sufentanil	26 (19)	25	57	166	3(12)/23(88)	46↘ (34)
Bolus ketamine	28 (20)	18	54	164	1(4)/27(96)	45↘ (34)

Values are presented as a number (%). ↗ indicates an increase, ↘ indicates a decrease.

Tab. 5. Mean administered doses of anesthetics according to groups of spinal deformities.

Groups	propofol	sufentanil	remifentanil
Total	6.07 mg/kg/h	0.44 µg/kg/h	0.21 µg/kg/min
AIS2	6.37 mg/kg/h	0.42 µg/kg/h	0.25 µg/kg/min
AIS3	6.31 mg/kg/h	0.43 µg/kg/h	0.22 µg/kg/min
AIS4	5.53 mg/kg/h	0.39 µg/kg/h	0.25 µg/kg/min
N	5.62 mg/kg/h	0.63 µg/kg/h	0.27 µg/kg/min
D	5.02 mg/kg/h	0.32 µg/kg/h	0.13 µg/kg/min
I	6.64 mg/kg/h	0.52 µg/kg/h	0.14 µg/kg/min

Values are presented as a number.

Electrophysiology data analysis

Intraoperative neuromonitoring was performed according to international guidelines. Baseline MEPs were obtained after positioning the patient. The IONM was performed with a Medtronic Dantec KeyPoint EMG/EP 4 channel amplifier and 2 channel stimulator. Tc-MEPs were generated by a multipulse generator and delivered to two sensory needle electrodes (28G) placed over the C3 and C4 motor cortical regions according to the international 10-20 system. Electrical stimulation was set to 100mA, 2.5 ms and an amplitude of 0.1Hz in all patients. Electromyographic responses were recorded from pre-gelled surface-patched electrodes placed bilaterally on the tibialis anterior muscle and the abductor hallucis muscle. Waveforms measured in µV were recorded and evaluated on Medtronic Dantec KeyPoint.net software. Input impedance of stimulating and recording electrodes was usually maintained below 5kΩ. We took actions to recover deteriorated MEPs as shown by other authors (28–33). We reviewed the MEP records from the lower extremities and investigated the change of amplitude from the baseline to the end of IONM in all spinal deformity groups

(Tab. 6). Also, we aimed the amplitude recording in groups with boluses of sufentanil and ketamine after an interval of 30 minutes.

Data analysis

The data were analyzed to allocate the incidence of neuromonitoring intraoperative changes in correlation to anesthesia. We considered all amplitude changes that occurred. We compared the differences in the groups. The main point of this study was to compare the remifentanil and sufentanil groups and the groups with bolus of sufentanil and bolus of ketamine. Our suspicion of statistically significant results was considered with the Fisher f-test and students t-test, we also used the ANOVA test for larger groups (34). Values of probability p-value lower than 0.05 were considered statistically significant. All analyses were performed using Microsoft Excel 2007 with the Analysis ToolPak.

Results

In our comprehensive study, we retrospectively observed and analyzed several groups with different anesthetic regimens over 10 years. We compared magnitudes of tc-MEP waveforms and anesthetic regimens (Tabs 7–10). We were interested in identifying specific groups with significant associations as follows.

Anesthesia regimen in association with tc-MEP, outcome

There were no significant differences in tc-MEP amplitude change between the groups of propofol (13 % increase), remifentanil (22 % increase), and sufentanil (26 % increase, p < 0.01). Significant differences were found between the groups of propofol,

Tab. 6. Spinal deformity groups and neurological deficit subgroup in dependence on tc-MEPs.

Deformity types	Number of patients (n)	Age mean (years)	tc-MEP waveform					
			mean base (µV)	mean end (µV)	max. base/end (µV)	min. base/end (µV)	absolute change (µV)	µV change base-end line
Total	139(100)	27	203	225	578/443	55/9	22↗	13 %↗
AIS2	64(46)	17	218	301	928/1195	5/4	83↗	41 %↗
AIS3	27(19)	19	186	165	793/596	14/5	21↘	7 %↘
AIS4	3(2)	16	218	0	218/0	218/0	218↘	75 %↘
N	8(6)	19	149	95	419/205	25/29	53↘	8 %↘
D	16(12)	55	122	107	490/418	9/10	15↘	6 %↘
I	21(15)	51	285	70	619/243	58/7	216↘	73 %↘
ND	43(31)	48	156	101	424/418	17/8	55↘	35 %↘

Values are presented as a number (%). Baseline mean value and endline of tc-MEPs. Absolute change column indicates ↗ amplitude increase or ↘ amplitude decrease of tc-MEPs from the beginning to the endline. In the ND subgroup we didn't consider tc-MEPs with no amplitude

Tab. 7. Anesthesia regimen in association with/without tc-MEPs between spinal deformities.

Anesthetics	AIS2	AIS3	AIS4	N	D	I	ND	Total
				mean tc-MEP magnitude baseline/endline				
Propofol								
TA l.sin.	83↗(40)	16↘(11)	0(0)	44↗(78)	37↘(37)	80↘(37)	25↘(34)	42↗(24)
AH l.sin.	99↗(65)	72↘(31)	266↘(100)	102↘(70)	46↗(57)	240↘(76)	27↘(24)	21↗(12)
TA l.dx.	87↗ (37)	34↗(28)	488↘(100)	41↗(34)	37↘(24)	212↘(88)	12↘(22)	38↗(19)
AH l.dx.	62↗ (22)	28↘(12)	118↘(100)	196↘(72)	33↘(21)	330↘(90)	65↘(17)	11↘ (4)
mean	83↗ (41)	21↘(7)	218↘(100)	53↘(8)	15↘(6)	216↘(73)	32↘(24)	22↗(13)
				without tc-MEP response (no amplitude presence) baseline/endline				
	Number of patients (%)							
TA l.sin.	2(3)/9(14)	6(22)/8(30)	3(100)/3(100)	1(13)/2(25)	6(38)/6(38)	13(62)/12(57)	20(47)/22(51)	32(23)/48(35)
AH l.sin.	3(5)/8(13)	4(15)/4(15)	2(67)/2(67)	1(13)/1(13)	5(31)/5(31)	13(62)/12(57)	19(44)/20(47)	29(21)/39(28)
TA l.dx	3(5)/4(6)	4(15)/3(11)	2(67)/2(67)	2(25)/3(38)	6(38)/6(38)	12(57)/12(57)	20(47)/19(44)	30(22)/36(26)
AH l.dx.	4(6)/9(14)	4(15)/3(11)	2(67)/2(67)	2(25)/3(38)	5(31)/5(31)	12(57)/12(57)	20(47)/18(42)	30(22)/42(30)
Total base/end line	5 %/12 %	17 %/17 %	75 %/75 %	19 %/28 %	34 %/34 %	21 %/24 %	46 %/46 %	30(22 %)/41(30 %)
Total mean	8 %	17 %	75 %	23 %	34 %	58 %	46 %	26 %
Tc-MEP depend. on time								
µV/anesthesia time	52↗/287	26↘/317	218↘/370	71↘/358	25↘/264	151↘/237	45↘/279	73↘/288
µV/minute	0.18↗	0.08↘	0.59↘	0.20↘	0.10↘	0.64↘	0.16↘	0.25↘
				mean tc-MEP magnitude baseline/endline				
Remifentanil								
TA l.sin.	27↗(15)	21↘(16)	0↘ (0)	4↗(8)	65↘(55)	9↗(7)	28↘(15)	5↗(3)
AH l.sin.	50↗(36)	81↘(37)	0↘(0)	90↘(79)	31↘(33)	218↘(77)	25↘(14)↗	13↘(8)
TA l.dx.	82↗ (41)	59↗(59)	0↘(0)	29↗(31)	93↘(58)	349↘(93)	28↘(15)	24↗(14)
AH l.dx.	3↗ (1)	25↗(13)	0↘(0)	115↘(55)	58↘(35)	466↘(93)	100↘(21)	32↘ (12)
mean	41↗ (23)	4↘(5)↗	0↘(0)	43↘(24)	62↘(45)	256↘(64)	45↘(9)	4↘(22)↗
				without tc-MEP response (no amplitude presence) baseline/endline				
	Number of patients (%)							
TA l.sin.	0(0)/2(7)	2(13)/4(27)	1(100)/1(100)	0(0)/1(33)	5(38)/6(46)	9(75)/9(75)	11(44)/13(52)	17(23)/24(32)
AH l.sin.	0(0)/2(7)	1(7)/1(7)	1(100)/1(100)	0(0)/0(0)	4(31)/5(38)	9(75)/9(75)	10(40)/12(48)	15(20)/19(25)
TA l.dx.	0(0)/2(7)	1(7)/0(0)	1(100)/1(100)	0(0)/1(33)	5(38)/6(46)	8(67)/8(67)	10(40)/11(44)	15(20)/19(25)
AH l.dx.	0(0)/1(3)	1(7)/0(0)	1(100)/1(100)	0(0)/1(33)	4(31)/5(38)	8(67)/8(67)	9(36)/10(40)	14(19)/18(24)
Total base/end line	0 %/6 %	8 %/8 %	100%/100%	0 %/25 %	35 %/42 %	71 %/71 %	40 %/46 %	15(20 %)/20(27 %)
Total mean	3 %	8 %	100%	13 %	38 %	71 %	43 %	24 %
Tc-MEP depend. on time								
µV/anesthesia time	27↗/298	1↘/323	0↘/360	65↘/340	65↘/261	207↘/228	66↘/267	62↘/288
µV/minute	0.09↗	0.004↘	0↘	0.19↘	0.25↘	0.91↘	0.25↘	0.22↘

Values are presented as a number (%). The difference between the baseline mean value and the endline of tc-MEPs. ↗ amplitude increase, ↘ amplitude decrease. Anesthesia time in minutes.

remifentanil, and sufentanil (magnitude increase 20 %) and bolus sufentanil (30 % decrease of magnitude), and bolus ketamine (730 % increase, p < 0.008). Major differences were observed between bolus sufentanil (30 % decrease of magitude) and bolus ketamine (730 % increase of magnitude, p < 0.001).

Anesthesia regimen in association without tc-MEP amplitude presence, outcome, percentage of patients

No significant difference was found between the groups of propofol (26 %), remifentanil (24 %), and sufentanil (28 %, p < 0.007). Considerable difference was found between the groups of propofol, remifentanil, and sufentanil (mean 26 %) and the group where ketamine boluses were administered. We didn't observe any loss of amplitude (0 %, p < 0.0002). In each comparison (propofol, remifentanil, and sufentanil) of the AIS2 and AIS3 groups (13 %)

and between the AIS4, I, and ND groups, we found a higher incidence of no amplitude presence (61 %, p < 0.02).

Anesthesia regimen in association with spinal deformity along with tc-MEP amplitude changes, outcome

Significant similarity was found between the groups of propofol, remifentanil, and sufentanil and AIS3 and 4, N, D, I, and ND (p < 0.009). Difference was found in the groups of propofol, remifentanil, and sufentanil in AIS2 (41 % amplification of magnitude, p < 0.04) as compared to the groups of propofol, remifentanil, and sufentanil in AIS3 and 4, N, D, I, and ND (28 % decrease of magnitude). In all anesthesia groups (propofol, remifentanil, and sufentanil), significant decreases of tc-MEP amplitude were found in groups AIS4 and I (74 %, p < 0.0001) compared to groups AIS2 and 3, N, D, ND.

Tab. 8. Anesthesia regimen in association with/without tc-MEPs between spinal deformities.

Anesthetics	AIS2	AIS3	AIS4	N	D	I	ND	Total
	mean tc-MEP magnitude baseline/endline							
Sufentanil								
TA l.sin.	148↗(64)	11↘(6)	0(0)	70↗(114)	111↗(287)	147↘(52)	22↘(64)	89↗(43)
AH l.sin.	151↗(92)	64↘(25)	0↘(0)	107↘(62)	613↗(3606)	261↘(76)	29↘(83)	63↗(33)
TA l.dx.	89↗ (34)	8↘(5)	0↘(0)	53↗(36)	163↗(129)	78↘(70)	10↗(35)↘	51↗(22)
AH l.dx.	132↗ (49)	115↘(38)	0↘(0)	272↘(81)	75↗(80)	195↘(84)	16↘(8)	19↗ (7)
mean	130↗ (59)	50↘(19)	0↘(0)	64↘(1)	240↗(1026)	170↘(71)	14↘(48)	55↗(26)
	without tc-MEP response (no amplitude presence) baseline/endline							
	Number of patients (%)							
TA l.sin.	2(6)/7(21)	4(36)/4(36)	2(100)/2(100)	1(20)/1(20)	1(33)/0(0)	4(44)/3(33)	9(50)/9(50)	15(23)/24(38)
AH l.sin.	3(9)/6(18)	3(27)/3(27)	1(50)/1(50)	1(20)/1(20)	1(33)/0(0)	4(44)/3(33)	9(50)/8(44)	14(22)/20(31)
TA l.dx.	3(9)/2(6)	3(27)/3(27)	1(50)/1(50)	2(40)/2(40)	1(33)/0(0)	4(44)/4(44)	10(56)/8(44)	15(23)/17(27)
AH l.dx.	4(12)/8(24)	3(27)/3(27)	1(50)/1(50)	2(40)/2(40)	1(33)/0(0)	4(44)/4(44)	11(61)/8(44)	16(25)/24(38)
Total base/endline	9 %/17 %	30 %/30 %	63 %/63 %	30 %/30 %	33 %/0 %	44 %/39 %	54 %/46 %	15(23 %)/21(33 %)
Total mean	13 %	30 %	63 %	30 %	17 %	42 %	50 %	28 %
Tc-MEP depend. on time								
μV/anesthesia time	75↗/277	64↘/310	218↘/375	75↘/368	95↗/278	104↘/250	18↘/296	18↗/289
μV/minute	0.270↗	0.207↘	0.581↘	0.204↘	0.343↗	0.415↘	0.062↘	0.063↗

Values are presented as a number (%). The difference between the baseline mean value and endline of tc-MEPs. ↗ amplitude increase, ↘ amplitude decrease. Anesthesia time in minutes.

Tab. 9. Anesthesia regimen in association with/without tc-MEPs between spinal deformities.

Anesthetics	AIS2	AIS3	AIS4	N	D	I	ND	Total
	mean tc-MEP baseline/30min							
Bolus sufentanil								
TA l.sin.	107↘(54)	68↘(70)	0(0)	579↘(52)	21↘(47)↗	111↘(52)	144↘(49)	109↘(49)
AH l.sin.	52↘(50)	79↘(45)	0↘(0)	65↘(10)	21↘(61)	243↘(77)	81↘(58)	71↘(50)
TA l.dx.	71↘ (30)↗	74↘(55)	0↘(0)	255↘(34)	90↗(36)	210↘(87)	76↘(36)	77↘(1)
AH l.dx.	121↘ (1)↗	240↘(68)	0↘(0)	1746↘(75)	24↗(18)	328↘(89)	280↘(45)	216↘ (24)
mean	88↘ (17)	115↘(60)	0↘(0)	661↘(43)	18↗(10)	223↘(76)	145↘(47)	118↘(30)
	without tc-MEP response (no amplitude presence) baseline/30min							
	Number of patients (%)							
TA l.sin.	2(13)/2(13)	0(0)/3(50)	0(0)/0(0)	0(0)/0(0)	0(0)/1(50)	0(0)/0(0)	1(10)/4(40)	2(8)/6(23)
AH l.sin.	2(13)/3(20)	0(0)/1(17)	0(0)/0(0)	0(0)/0(0)	0(0)/1(50)	0(0)/0(0)	1(10)/3(30)	2(8)/5(19)
TA l.dx.	1(7)/2(13)	0(0)/1(17)	0(0)/0(0)	0(0)/0(0)	0(0)/0(0)	0(0)/0(0)	1(10)/1(10)	1(4)/3(12)
AH l.dx.	2(13)/6(40)	0(0)/1(17)	0(0)/0(0)	0(0)/0(0)	0(0)/0(0)	0(0)/0(0)	1(10)/1(10)	2(8)/7(27)
Total base/30min	12 %/12 %	0 %/13 %	0 %/0 %	0 %/0 %	0 %/13 %	0 %/0 %	10 %/18 %	2(7 %)/5(11 %)
Total mean	12 %	6 %	0 %	0 %	6 %	0 %	14 %	9 %
Tc-MEP dependent on time								
μV/30min anesthesia time	88↘/30	115↘/30	0↘/0	661↘/30	18↗/30	223↘/30	145↘/30	214↘/30
μV/minute	2.92↘	3.83↘	0↘	22.04↘	0.60↗	7.43↘	4.84↘	7.13↘

Values are presented as a number (%). The difference between the baseline mean value and after 30 minutes of tc-MEPs. ↗ amplitude increase, ↘ amplitude decrease. Anesthesia time in minutes.

Anesthesia regimen in association with anesthesia time along with tc-MEP amplitude change, outcome

The average amplitude of tc-MEPs decreased in the groups of propofol, remifentanil, and sufentanil (35 % decrease of magnitude) during the average 288 minutes of anesthesia time. We didn't consider 2 patients in sufentanil group D because of tc-MEP excitability.

Deformity types in association with tc-MEP changes, outcome

In this group, there were 139 patients (100 %) divided into spinal deformity subgroups (Table 2). Significant differences appeared in age between groups AIS2-4, and N (18 years old) and groups D, I, and ND (51 years old, p < 0.0005). Sex differences were observed in scoliotic groups AIS2-4, N, and D (88 % F) and group I without scoliotic deformities (52 % F, p < 0.001). Tc-MEP differences were found between groups AIS2 (magnitude increase 41 %) and AIS3, AIS4, N, D, and I (mean magnitude decrease 34 %, p < 0.02). Major differences were found between groups AIS2 and 3, N, and D (mean magnitude increase 5 %) and groups AIS4 and I (mean magnitude decrease 74 %, p < 0.004) (Tab. 6).

Tab. 10. Anesthesia regimen in association with/without tc-MEPs between spinal deformities.

Anesthetics	AIS2	AIS3	AIS4	N	D	I	ND	Total
	mean tc-MEP baseline/30min							
Bolus ketamine								
TA l.sin.	197↗(310 %)	52↗(67)	0(0)	732↗(247)	0(0)	99↘(19)	257↗(200)	195↗(278)
AH l.sin.	146↗(188)	2↘(4)	0 (0)	440↘(72)	0(0)	75↘(18)	13↗(152)	107↗(157)
TA l.dx.	235↗(1289)	38↗(36)	0 (0)	2256↗(738)	0(0)	10↗(11)	442↗(154)	285↗(1136)
AH l.dx.	243↗ (1558)	14↗(31)	0 (0)	522↘(56)	0(0)	14↗(350)	47↘(68)	191↗ (1348)
mean	205↗ (836)	25↗(33)	0 (0)	507↗(226)	0(0)	38↘(81)	166↗(143)	195↗(730)
	without tc-MEP response (no amplitude presence) baseline/30min							
	Number of patients (%)							
Total base/30min	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
Tc-MEP dependent on time								
μV/30min anesthesia time	205↗/30	25↗/30	0/0	507↗/30	0/0	38↘/30	166↗/30	195↗/30
μV/minute	6.84↗	0.84↗	0	16.88↗	0	1.25↘	5.54↗	6.48↗

Values are presented as a number (%). The difference between the baseline mean value and after 30 minutes of tc-MEPs. ↗ amplitude increase, ↘ amplitude decrease. Anesthesia time in minutes. Bolus ketamine table doesn't have patients without a tc-MEP response.

Neurological deficit, anesthesia, outcome, percentage of patients

The success rate of tc-MEP recording according to the neurological deficit group in the propofol, remifentanil, and sufentanil groups was 17 % in MRC 3, 96 % in MRC 4, and 87 % in MRC 5. In the neurological deficit (ND) group without tc-MEP amplitude, the response mean was 46 % patients in the propofol, remifentanil and sufentanil groups.

Discussion

Intraoperative neurophysiological monitoring using tc-MEPs is routinely employed in spinal surgery, particularly for procedures involving scoliosis correction, spinal neoplasms and other spinal deformities. There are known limitations to IONM. Multiple non-neurological related factors can affect the waveforms, such as blood pressure, heart rate, temperature, partial pressure of alveolar carbon dioxide, and anesthetic drugs (4). In addition, challenging clinical conditions, such as severe myelopathy, obesity, or peripheral neuropathy can make interpretation difficult or even impossible (35). In our study we observed that in the group with neurological deficit (ND) no tc-MEPs appeared in 20 patients (14 %) out of a total of 139 patients (100 %). This 14 % of patients divided into subgroups where 13 patients (9 %) had a new neurological deficit and the other 7 patients (5 %) didn't experience any new change in neurological deficit. Other studies have also found similar results. Clark et al (36) found that neurophysiological alerts were present in 16 patients (11 %) out of a total of 140 patients. Overall, 8 patients (6 %) experienced new postoperative neurological deficits. There was a significant association between IONM MEP alerts and the presence of a new postoperative deficit.

In studies of patients undergoing scoliosis surgery, the incidence of a significant intraoperative monitoring change has been reported to occur from 3.6 % to 8.7 % (37–39). Another study recorded an increased incidence of 11.8 % of patients with a neurological deficit before surgery worsening postoperatively (25).

A total of 16 patients (17 %) recorded a successful response of tc-MEPs in our group with neurological deficit according to MRC grade 3. In another study, Lee et al (40) successfully obtained basal tc-MEP amplitude according to MRC grade 3 in 4 patients (28.6 %). Any muscle amplitude MEPs in the lower extremities was considered a successful recording.

Reports suggest that tc-MEP responses degrade or undergo anesthetic fade during surgery despite unchanged anesthetic levels and other physiologic variables (5). In a study by Ugawa et al (41), the amplitude of MEP significantly decreased in the lower limbs at 5 hours by 31 % and at 6 hours by 39 % after the initial infusion of propofol. Mean operating time was 282.1 minutes. We considered significant similarities in our study. Mean tc-MEP amplitude decreased in the groups of propofol, remifentanil and sufentanil by 35 % in an average of 288 minutes of anesthesia time (p < 0.04). Lonner et al (42) reported that the operating time for the treatment of adolescent idiopathic scoliosis was 180.2 min for experienced surgeons and 221.9 min for inexperienced surgeons. In comparison to our study group of adolescent idiopathic scoliosis AIS2, there was 287 min of anesthesia time. If we consider the real operating time it would be 204 min. In our study, the time between the induction of anesthesia and the surgery is on average 63 min. The time of surgery end and anesthesia end is on average 20 min.

Tc-MEPs tend to exhibit gradually rising thresholds during the hours of surgery. Sedative-hypnotics such as propofol cause unconsciousness by producing corticocortical inhibition, possibly by GABA-mediated (Gamma-aminobutyric acid) inhibitory interneuron activity within the cerebral cortex with minimal depression of spinal alpha motor neurons. Propofol produces a dose-dependent depression of tc-MEP responses.

The mechanism of action of ketamine (ket) is rather complex. Moderate doses of ket are thought to increase motor excitability by blocking *N*-methyl-D-aspartate (NMDA) receptor-mediated excitatory inputs to inhibitory interneurons (18, 43, 44). Furmaga et al (19) found in their study that cortical excitability, as indexed by the amplitude of MEPs, was higher under ket than propofol. Our study showed retrospectively that administration of a 30mg ketamine bolus during surgery increased the tc-MEP amplitude after mean 30 minutes to 195 μV (730 %).

In older groups, the success rate can decrease due to peripheral neuropathy or age-related disorders (40). In our study, we confirmed this statement. The group of patients in AIS2, with a mean age of 17, had 2 patients (3 %) with neurological deficit and no tc-MEP amplitude in 5 patients (8 %). Overall, a significant increase of tc-MEP amplitude 83µV (41 %) was observed successfully in 59 patients (92 %, p < 0.0005). Older patients with a mean age of 51 in groups D, I, and ND underwent anesthetic fade of 38 % amplitude decrease.

Many cases in our study with significant tc-MEP alerts underwent an evidence-based response checklist (45).

Conclusion

We found that intraoperative neurophysiological monitoring can be performed with either way of TIVA: propofol, remifentanil and sufentanil, with no statistical difference. Significant findings were found in the administration of sufentanil boluses where the amplitude decreased and in ketamine boluses where the amplitude rose. We also confirmed the claims of anesthetic fade in tc-MEP amplitude during long surgery. Spinal deformities with more severe curves had a magnitude decrease. In older patients and neurologic deficit patients we also found the same situation.

The effect of anesthetics on tc-MEPs is dose and time dependent. The usefulness of IONM is dependent on patient samples and accurate evaluation of tc-MEPs. The roles of the spinal surgeon, anesthesiologist and neurophysiologist are to cooperate in early recognition of tc-MEP change and find an accurate method to ensure the best neurological outcome.

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