

Pre-Operational and Post-Operational Motor Stimulated Potential, Electrophysiological Conduction Studies in Patients with Tethered Cord Syndrome, Neurological Examination and Comparison of Lumbosacral MRG Investigations

Gergin Omurilik Sendromlu Hastalarda Preop ve Postop Motor Uyarılmış Potansiyel, Elektrofizyolojik İletim Çalışmaları, Nörolojik Muayene ve Lumbosakral MRG Tetkiklerinin Karşılaştırılması

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ABSTRACT

Objective: In the current study, we aimed to define the potential of pre-op motor evoked potentials (MEP) to predict the response to surgical treatment and the change of MEP values after surgery among the subjects with the diagnosis of Tethered cord syndrome (TCS).

Material and Method: In this prospective study, 20 adult subjects (15 females, 5 males) with an average age of 35.6 were included. Pre-operative (pre-op) and post-operative (post-op) physical and neurological examinations, motor evoked potentials (latency, amplitude) and nerve conduction studies were performed on all subjects diagnosed with TCS. Pre-operative (pre-op) and post-operative (post-op) physical and neurological examinations, motor evoked potential and nerve conduction studies were performed on all subjects diagnosed with TCS. Upper extremity median and upper nerve sensory and motor conduction studies and lower extremity sural nerve sensory and tibialis posterior and peroneal nerve motor nerve conduction studies were performed antidromically with Standard method in all subjects

Results: After surgery, 15 out of 20 patients showed a significant clinical improvement. Thus, subjects were categorized into two groups: 15 patients who recovered after surgery were in Group 1, and 5 patients who did not show any clinical improvement in Group 2. Even Though it did not reach statistical significance, cortical- Abductor Pollicis Brevis (APB) and cervical-APB latency values at the initial evaluation were higher in Group 2 (p values 0.050 and 0.052, respectively). Among the subjects in Group 1, cortical-APB latency, cervical-APB latency and CMCT (central motor conduction time) lower values improved prominently (p values, 0.031, 0.010, and 0.043, respectively).

Conclusion: Cortical-APB latency, cervical-APB latency and CMCT values might be useful for the follow-up of the patients with TCS, while cortical-APB latency and cervical-APB latency values could be a good predictor to define who might be of benefit from the surgery.

Keywords: Tethered cord syndrome, Surgery, Motor evoked potentials

ÖZET

Giriş: Bu çalışmada, Gergin omurilik sendromu (GOS) tanılı olgularda ameliyat öncesi motor uyarılmış potansiyellerin (MUP) cerrahi tedaviye yanıtı öngörme potansiyelini ve ameliyat sonrası MUP değerlerinin değişimini tanımlamayı amaçladık.

Materyal ve Metot: Bu gözlemsel kohort çalışmasına, yaş ortalaması 35.6 olan 20 yetişkin olgu (15 kadın, 5 erkek) dahil edildi. GOS tanısı konulan tüm olguların ameliyat öncesi (pre-op) ve sonrası (post-op) fizik ve nörolojik muayeneleri, motor uyarılmış potansiyelleri (latans, amplitüd) ve sinir iletim çalışmaları yapıldı. GOS tanısı alan tüm olguların ameliyat öncesi (pre-op) ve ameliyat sonrası (post-op) fizik ve nörolojik muayeneleri, motor uyarılmış potansiyel ve sinir iletim çalışmaları yapıldı. Üst ekstremité median ve üst sinir duyu ve motor iletim çalışmaları ve alt ekstremité sural sinir duyu ve tibialis posterior ve peroneal sinir motor sinir iletim çalışmaları tüm olgularda Standart yöntemle antidromik olarak yapıldı

Bulgular: Ameliyattan sonra, 20 hastanın 15'i anlamlı bir klinik iyileşme gösterdi. Böylece, olgular iki gruba ayrıldı: Ameliyattan sonra iyileşen 15 hasta Grup 1'de ve klinik iyileşme göstermeyen 5 hasta Grup 2'de yer aldı. İstatistiksel anlamlılığa ulaşmasa da, ilk değerlendirmede kortikal-Abductor Pollicis Brevis (APB) ve servikal-APB latans değerleri Grup 2'de daha yüksekti (p değerleri sırasıyla 0.050 ve 0.052). Grup 1'deki olgular arasında kortikal-APB latansı, servikal-APB latansı ve CMCT (merkezi motor iletim süresi) alt değerleri belirgin şekilde iyileşmiştir (p değerleri sırasıyla 0.031, 0.010 ve 0.043).

Sonuç: Kortikal-APB latansı, servikal-APB latansı ve CMCT değerleri GOS'lu hastaların takibinde faydalı olabilirken, kortikal-APB latansı ve servikal-APB latansı değerleri cerrahiden fayda görebilecek hastaları belirlemede iyi bir belirleyici olabilir.

Anahtar kelimeler: Gergin kord sendromu, Cerrahi, Motor uyarılmış potansiyeller

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INTRODUCTION

Tethered cord syndrome (TCS) is a progressive neurologic disorder which is a result of hypoxia that occurs due to a stretching of spinal cord (Umur et al., 2007). Before the widespread use of MRI, TCS was frequently overlooked in adults, typically presenting with lower extremity motor-sensory changes, pain, scoliosis, or sphincter dysfunction (Hoffman et al., 1976; Menezes et al., 2021).

TCS, in which the conus medullaris ends at a level below the L1-2 intervertebral space, is considered to be stretched when the spinal cord is thick phylum terminal or low conus medullaris (Selçuki et al., 2003). Warder and Oakes reported that the normal localization of the caudal end of spinal cord was found in 18% of adults and children with TCS (Warder et al., 1993). The antero-posterior diameter of the filum terminale is measured at the L5-S1 level in axial sections in MRI and should be below 2 mm (Hall et al., 1988). MRI is not only useful in diagnosis of TCS, but also in revealing the etiological factor that causes tension (Halevi et al., 2011).

Since there is no reliable method to predict symptom onset, relying solely on follow-up—especially in children who have not completed their growth—may carry risks despite initial asymptomatic presentation (Halevi et al., 2011). Given the fact that the symptoms other than pain rarely improve spontaneously, the importance of prophylactic surgery is apparent. The main purpose of the treatment of TCS is to eliminate the pathology that causes stretching of the spinal cord. In this way, it is thought that early elimination of metabolic disorder in the medulla spinalis, venous congestion due to local hypoxia and reduction in the number of mitochondria is effective in the improvement of clinical findings (Yamada et al., 1981). Since the tension is relieved in adult patients who are diagnosed before the symptoms appear and underwent an appropriate surgery, clinical findings usually do not occur. It was also reported that among the patients who are diagnosed before the symptoms appear and underwent appropriate surgery, clinical findings are usually absent (Selçuki, 2011).

The diagnosis of TCS is mostly clinical and MRI, somatosensory evoked potentials (SEP) and urodynamics are diagnostic methods (Barkovich, 1996; Ross et al., 2010). Electromyography (EMG), in particular pelvic floor EMG (for external urethral sphincter activity) and external anal sphincter EMG, cannot be performed widely due to technical factors among the children. In addition, although fibrillation potentials are seen in EMG in patients with TCS, this situation is not specific for TCS (Yamada et al., 2001).

Electrical stimulation of the spinal roots can also be used as an examination method (Seçil et al., 2012). Transcranial magnetic stimulation (TMS) is a technique of neuro-stimulation and neuro-modulation based on the principle of an electromagnetic induction in the brain (Kobayashi et al., 2003). Information obtained from TMS studies helps to identify lesions in the nervous system and distinguish between axonal or predominantly demyelinating pathology in motor pathways and also helps to predict functional motor outcome after injury. The abnormalities revealed by TMS are not disease specific and results should be interpreted with other clinical variables.

Motor evoked potentials (MEP) provide information about excitability of the motor cortex, functional integrity of intra-cortical neuronal structures, conduction along cortico-spinal, cortico-nuclear and callosal fibers, function of nerve roots and pathways from peripheral nerves to muscles (Lefaucheur, 2019). By using MEP, valuable information about the cortico-spinal tract and thus the lateral column is obtained in spinal cord diseases and it facilitates functional diagnosis. At the same time, information about local or general motor root involvement can be obtained by magnetic stimulation of the cervical and lumbar spinal roots. If the lesion affects the posterior cord, SEPs are found abnormal in lesions affecting the lateral cord and MEPs.

In this study, we aimed to examine the potential of pre-op MEP values to predict response to surgical treatment in subjects with TCS and the role of MEP values in the follow-up of surgically treated TCS subjects.

MATERIAL and METHOD

In this prospective study was carried out in Celal Bayar University Neurology and Neurosurgery Clinics from 28-03-2012 to 15-04-2014 in Manisa Türkiye. 20 adult subjects (15 females, 5 males) with an average age of 35.6, who were admitted to the neurology and neurosurgery clinics of Celal Bayar University (CBU) and diagnosed with TCS by clinical, neuro-imaging, and SEPs were included in our study.

Pregnant women, patients with mental retardation, patients under 18 years of age, patients with previous brain or spinal cord surgery, epilepsy patients, using biomedical devices such as cardiac pacemakers, aneurysm clips, and cases with motor polyneuropathy were excluded from the study.

The subjects were not receiving any treatments. All of the subjects participating in the study were informed about the study in detail and signed a consent form.

Preoperative (pre-op) and post-op (post-op) physical and neurologic examinations, motor evoked potential and nerve conduction studies were performed in all patients diagnosed with TCS. Upper extremity median and superior nerve sensory and motor conduction studies and lower extremity sural nerve sensory and tibialis posterior and peroneal nerve motor conduction studies were performed antidromically with standard methods in all cases (Oh, 2003).

All upper and lower extremity conduction studies were within normal ranges according to the gender and age-matched values used by our laboratory (Ertekin, 2006). MEP and TMS measurements in the study were performed using a 1998 model Magiclife brand Transcranial Stimulation device and a 2000 model Dantec brand EMG device connected to this device in the electrophysiology laboratory of CBU neurology department.

The procedure was performed in a quiet, brightly lit room with the patient lying supine on a stretcher with his/her head slightly elevated, eyes open and awake. The amplifier filters of the device were set to frequency 1-10 Hz, 100 microseconds, 3 tesla magnetic field was generated with a single stimulus. For recording, the active electrode was placed on the proximal 1/3 of the abductor pollicis brevis (APB) muscle in the tenar region in the upper extremity, on the tibialis anterior (TA) muscle in the lower extremity; inactive electrodes were placed on the tendon 2-5 cm apart from the active bar electrode. To obtain the right MEP, the stimulating round coil was placed 45 degrees lateral to the left from the Cz point on the scalp for the upper extremity and at the vertex for the lower extremity.

Electromagnetic stimulation was applied from C7 in the cervical region and L4 in the lumbar region through the foraminal (Groppa et al., 2012). In patients with no response or low amplitude, the procedure was repeated as many times as necessary by changing the location of the stimulating coil in order to find the maximal stimulation area (sweet spot). MEP values were recorded from the abductor pollicis brevis muscle and Tibialis ant muscle. MEP amplitude was obtained in millivolts (mV) and MEP latency in milliseconds (msn).

Pre-op and post-op upper extremity cortical-APB latency and amplitude, cervical-APB latency and amplitude, lower extremity cortical-TA latency and amplitude, lumbar-TA latency and amplitude values were obtained with MEP obtained by recording from distal muscles of upper and lower extremities.

In our study, the central motor conduction time (CMCT) was obtained for the upper and lower extremities by subtracting the MEP latency obtained

by cortical stimulation in pre-op and post-op subjects, and by subtracting the MEP latency obtained by anterior root stimulation. Motor threshold values were 65% and 70% for the lower extremities.

Ethical considerations

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Research Ethics Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The ethical approval of the study was obtained from the Ethics committee of Celal Bayar University Faculty of Medicine (Date: 28/03/2012, Decision Number: 2012/118).

Statistics

The data obtained in the study were analyzed using SPSS 15.0. Descriptive and interpretative statistical analyzes of the data are given in the form of tables. It was determined that the data were statistically normally distributed. For the baseline comparison between groups (Group 1 vs. Group 2), the Independent Samples t-test was used for continuous variables. For comparing categorical variables such as gender distribution between groups, the Chi-square test was used. Pre-op and post-op motor excitation potential values of the patients were compared with Paired Samples t-test and with the average reference values in the laboratory with Single-sample T-Test. In interpretative statistical comparisons, $\alpha = 0.05$ confidence interval was selected and the difference between the compared groups was considered statistically significant if the "p" value was less than 0.05.

RESULTS

All the subjects had low back, perineum, or leg pain at the time of initial admission. Eleven (55%) of the subjects had urinary incontinence and 1 (5%) had stool incontinence.

A decrease in post-op TCS complaints was detected in 15 patients (75%). Stool incontinence was found to be improved in one subject. However, three out of 11 subjects with urinary incontinence did not present any improvement.

Lumbar magnetic resonance imaging of all patients showed no preop-postop changes.

The two groups were similar in terms of gender distribution and age (p values 0.366 and 0.495, respectively) (Table 1). There was no statistical difference between the groups in pre-op measurements. However, although pre-op cortico-APB latency and cervical-APB latency values were high in the second group, this difference did not reach statistical significance (0.050 and 0.052).

Table1. The demographic characteristics of the subjects

	Group 1 (N: 15)	Group 2 (N: 5)	P value*
Sex, male, N (%)	3 (20%)	2 (40%)	0.366#
Age, median, years old (SD)	34.4 (3.5)	39 (2.8)	0.495
Pre-op Cortical-APB lat (ms), mean (SD)	19.8 (0.6)	22.4 (0.6)	0.050
Pre-op Cervical-APB lat (ms), mean (SD)	12.4 (0.3)	13.8 (0.5)	0.052
Pre-op Cortical-APB amp(mV), mean (SD)	3.0 (0.5)	5.1 (1.0)	0.100
Pre-op Cervical-APB amp(mV), mean (SD)	6.9 (1.5)	2.6 (1.1)	0.133
Post-op Cortical -TA lat(ms), mean (SD)	26.3 (1.0)	28.5 (1.2)	0.286
Post-op Lomber-TA lat(ms), mean (SD)	13.0 (0.6)	11.6 (0.8)	0.295
Post-op Cortical-TA amp(mV), mean (SD)	0.9 (0.1)	1.6 (0.3)	0.074
Post-op Lomber-TA amp(mV), mean (SD)	1.6 (0.3)	2.0 (0.7)	0.547
Post-op CMCT upper (ms), mean (SD)	7.3 (0.5)	8.5 (0.8)	0.296
Post-op CMCT lower (ms), mean (SD)	13.3 (1.0)	16.5 (0.8)	0.112

Table 1. APB:Abductor pollicis brevis,TA:Tibialis anterior,Lat:Latency,Amp:Amplitude, mV:millivolts,ms: milliseconds CMCT: Central motor conduction time, SD: Standard deviation. * Independent Samples t-test. # Chi-square test

Group 1: TCS patients with clinical improvement after surgery

Group 2 : TCS patients with no clinical improvement after surgery. The decline in MEP values of cortico-APB latency, cervical-APB latency and CMCT lower

after surgery were statistically significant in Group 1 (p values, 0.031,0.010, and 0.043, respectively). In contrast, in Group 2, there was no significant improvement in any measurements (Table 2).

Table 2. Changes in MEP values according to treatment success after surgery in patients with TCS.

Values		The Change After Surgery, mean (SD)	P value*
Cortical-APB lat (ms)	Group 1 (N: 15)	-1.7 (2.8)	0.031
	Group 2 (N: 5)	0.78 (3.1)	0.611
Cervical- APB lat (ms)	Group 1 (N: 15)	-0.75 (0.98)	0.010
	Group 2 (N: 5)	0.68 (1.6)	0.415
Cortical-APB amp (mV)	Group 1 (N: 15)	-0.78 (2.53)	0.254
	Group 2 (N: 5)	0.46 (4.2)	0.821
Cervical-APB amp (mV)	Group 1 (N: 15)	-1.62 (8.1)	0.452
	Group 2 (N: 5)	0.66 (1.9)	0.484
Cortical-TA lat (ms)	Group 1 (N: 15)	-2.4 (5.1)	0.090
	Group 2 (N: 5)	0.38 (2.2)	0.730
Lomber-TA lat (ms)	Group 1 (N: 15)	0.82 (2.5)	0.229
	Group 2 (N: 5)	0.02 (2.2)	0.983
Cortical-TA amp (mV)	Group 1 (N: 15)	0.25 (0.5)	0.107
	Group 2 (N: 5)	0.06 (0.5)	0.821
Lomber-TA amp (mV)	Group 1 (N: 15)	0.36 (1.17)	0.248
	Group 2 (N: 5)	0.7 (1.2)	0.284
CMCT lat (ms) upper	Group 1 (N: 15)	-1.0 (2.7)	0.176
	Group 2 (N: 5)	0.1 (3.2)	0.948
CMCT lat (ms) lower	Group 1 (N: 15)	-3.2 (5.6)	0.043
	Group 2 (N: 5)	-0.04 (1.6)	0.960

APB:Abductor pollicis brevis,TA:Tibialis anterior,Lat:latency,Amp:amplitude, mV:millivolts,ms: milliseconds CMCT: Central motor conduction time, SD: Standard deviation. * Paired Samples t-test

Group 1: TCS patients with clinical improvement after surgery

Group 2 :TCS patients with no clinical improvement after surgery

As can be seen in Table 3, only the cortical -TA amplitude pre-post operation values of the patients' preop and postop motor evoked potential values

were significant compared to the laboratory mean reference values (p<0,05).

Except for these, no statistically significant difference was found in the comparison of all other values obtained according to the laboratory reference values.

Table 3. T-test result table for the comparison of preop and postop motor arousal potential values of the patients with the laboratory mean value

	N	Mean	lab normal values	SD	t	df	p*
Cortical-APB lat (ms) (Preop)	20	20,4900	21,38	2,62837	-1,514	19	0,146
Cortical-APB lat (ms) (Postop)	20	21,6250		2,43156	0,451	19	0,657
Cervical- APB lat (ms) (Preop)	20	12,8050	12,38	1,44677	0,325	19	0,749
Cervical- APB lat (ms) (Postop)	20	13,2000		1,66891	1,340	19	0,196
Cortical-APB amp (mV) (Preop)	20	3,5800	4,55	2,40867	-1,801	19	0,088
Cortical-APB amp (mV) (Postop)	20	4,0500		3,36804	-0,664	19	0,515
Cervical-APB amp (mV) (Preop)	20	5,8700	6,48	5,53088	-0,493	19	0,628
Cervical-APB amp (mV) (Postop)	20	7,2500		4,79435	0,718	19	0,481
Cortical-TA lat (ms) (Preop)	20	26,9050	27,80	3,95561	-1,012	19	0,324
Cortical-TA lat (ms) (Postop)	20	28,6400		3,42612	1,096	19	0,287
Cortical-TA amp (mV) (Preop)	20	1,1050	1,60	0,71926	-3,078	19	0,006*
Cortical-TA amp (mV) (Postop)	20	0,9000		0,63246	-4,950	19	0,000*
Lomber-TA lat (ms) (Preop)	20	1,7200	12,00	1,32490	0,608	19	0,551
Lomber-TA lat (ms) (Postop)	20	1,2700		1,55160	-0,778	19	0,446
Lomber-TA amp (mV) (Preop)	20	1,7200	1,54	1,32490	0,608	19	0,551
Lomber-TA amp (mV) (Postop)	20	1,2700		1,55160	-0,778	19	0,446
CMCT (ms) upper (Preop)	20	7,6850	8,57	2,15389	0,608	19	0,551
CMCT (ms) upper (Postop)	20	8,4250		1,95741	-0,778	19	0,446
CMCT (ms) lower (Preop)	20	14,1300	15,90	3,92805	-2,015	19	0,058
CMCT (ms) lower (Postop)	20	16,5850		3,00461	1,020	19	0,321

Table 3: APB:Abductor pollicis brevis,TA:Tibialis anterior,Lat:latency,Amp:amplitude, mV:millivolts,ms: milliseconds CMCT: Central motor conduction time, SD: Standard deviation, df: degree of freedom. * Single-sample T-Test.

DISCUSSION

Pre-op cortical-APB latency and cervical-APB latency values were found to be higher in Group 2 compared to Group 1. Although these values did not reach statistical significance, in our opinion this difference could reach statistical significance by increasing the number of subjects included into the study. There is a lack in the literature in terms of prognostic factors predicting the outcome of the surgery for TCS. Thus, this could be a promising result that the investigators could focus on in the further research.

Polo et al previously reported that the tension in the spinal cord affects the dorsal horn interneurons in the early period, and the other parts will be affected by the long-term tension (Polo et al., 1994). As a result of experimental studies using the animal traction model, histological examination of the stretched spinal cord segments showed that the most neuronal damage was in the central part of the lumbosacral region, including the area between neurons and the ends of the long paths (Canaz et al., 2018). In the study conducted by Canaz and colleagues, the results of 20 patients with myelomeningocele were examined, it was stated that although the level of conduction block in the motor pathways includes nerve roots in some cases, most of the stimulated roots are functional; the motor conduction block is at the upper levels of the spinal cord (Canaz et al., 2018).

When the deterioration in the interneurons potential is evaluated, the deterioration in the posterior column develops more rapidly during anoxia and the nerve cells in the spinal cord suffer from metabolic problems more quickly than the axons that need less energy. This result is supported by the histological studies of Van Harreveld et al (Harreveld et al., 1962).

Incontinence and muscle atrophy with decreased reflex response could be the early signs of TGC patients. However, findings such as increased reflex responses and Babinski's evidence together with muscle weakness, which are long tract findings, emerge in later periods (Yamada et al., 2001). In our study, the presence of pre-op incontinence was similar in the groups that responded to surgery and those who did not. The fact that the only patient with stool incontinence was in the group showing improvement supports this information. Late-term findings such as Babinski's evidence were not detected in any of our patients before the surgery.

In addition, in our study, a significant decrease was observed in the cortical-APB latency, cervico-APB latency and CMCT sub-values among Group 1 subjects. The improvement seen in the measurements after surgery may be due to the increase in regional blood flow and the improvement of ischemia in the tense area.

In a Doppler flow study, relieving tension provided a 3-fold increase in regional blood flow (Schneider et al., 1993). Previously, higher hypoxanthine and lipid peroxidation levels that may be related with ischemic damage in an animal study in which tense spinal cord was created. The study also revealed a significant delay in motor evoked potential and somatosensory evoked potential waves (Koçak et al., 1997).

On the other hand, clinical parameters are still the most reliable method recommended for the follow-up of patients with TCS after surgery (Hall et al, 1988). The place of MRI or repeated measurements in post-op follow-up is controversial (Halevi et al., 2011). It was shown that MRI imaging was insufficient to detect re-strain of the spinal cord 6-18 months after surgery among TCS patients. Similarly, in our study, we found that there was no significant difference in pre-op and post-op lumbosacral MRI imaging in terms of improvement of TCS. However, as of the importance of repeated measurements during follow-up after surgery, we found that there was a significant improvement especially in cortical-APB latency, cervical-APB latency and SMIZ sub-values.

Conclusion

Cortico-APB latency, cervical-APB latency, and CMCT values may not only predict post-operative recovery when measured preoperatively but also reflect clinical improvement during follow-up.

However, our study is limited by the small number of adult TCS patients included, as well as the short follow-up period. Further research involving a larger patient group and a longer follow-up period is required in this area.

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Material, methods and data collection: USS, MS;

Data analysis and comments: USS, DS, GYO;

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