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Clinical and Neurophysiological Correlation in Axonal and Demyelinating Polyneuropathy

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ABSTRACT

Introduction: *The neurophysiological examination provides valuable pathophysiological information for the diagnosis, prognosis and therapy of patients with polyneuropathy**(1).** Nerve conduction study (NCS) is the most objective and reliable measure of peripheral nerve function and is considered the gold standard for the diagnosis of mostneuropathies **(2 and 3).***

Aim of the Study: *To evaluate the clinical usefulness of nerve conduction study in the differentiation between axonal and demyelinating polyneuropathies andto correlate the neurophysiological results with the clinical findings in all patients.*

Patient and Methods: *In the present study, One hundred and twenty five patients with symptoms and signs of polyneuropathy were studied ranging in age from **9** years to **79** years.In total, thirty-six patients were classified as axonal polyneuropathy, twenty-three patients as demyelinating, and nine patients as mixed, while fifty-seven patients were classified as neuropathic.NCS and EMG were performed using Nihon Kochden electromyography machine with surface recording and stimulating electrodes. Nerve conduction studies were carried out at 33°C room temperature **(4).***

Results: *There is statistically significant linear correlation between reduction in SNAP amplitude and decrease in sensory CV of median and ulnar nerves. Also there is statistically significant inverse correlation between reduction in CMAP amplitude and increase in DML. There is statistically significant linear correlation between reduction in CMAP amplitude and decrease in motor CV There is statistically significant linear correlation between reduction in CMAP amplitude and decreased grade of power (MRC grade) in median, ulnar, peroneal and tibial nerves in both axonal and demyelinating polyneuropathy, statistically significant linear correlation was found between decrease in conduction velocity and decrease in grade of power.*

Conclusions: *The present study demonstrates significant correlation between amplitude reduction and conduction slowing in demyelinating as well as axonal polyneuropathy. Analysis of EMG findings in the present study showed no difference between axonal and demyelinating polyneuropathies as regardspontaneous activity assessment, interference pattern.*

Keywords: *Axonal Polyneuropathy-Demyelinating Polyneuropathy – Neurophysiology.*

INTRODUCTION

Polyneuropathy is a common disorder with heterogenic clinical presentation and many different etiologies. Neurophysiological examination plays an important role in defining the presence of a polyneuropathy and in terms of delineating the underlying pathophysiological process (i.e., primary axonal loss vs primary demyelination) ***(5)***.

Aim of the Work

To evaluate the clinical usefulness of conduction slowing and CMAP or SNAP amplitude reduction in the differentiation between axonal and demyelinating polyneuropathies. And to correlate the neurophysiological results with the clinical findings in all patients.

Patients and Methods

One hundred and twenty five patients with symptoms and signs of polyneuropathy **78 male (62.4%): 47 female (37.6%)**were studied ranging in age from **9** years to **79** years (**44.75 ± 17.66)**. Patients were questioned for sensory, motor and autonomic symptoms. A clinical history and full neurological examination were

obtained and incorporated when necessary from the patient's file, as well as all laboratory investigations. The patients were classified according to criteria proposed by the ESTEEM group***(6)***.

Control Group

The control group included 30healthy asymptomatic individuals **19 male (63.3%):11 female (36.7%)** with no history of diabetes or other systemic diseases with mean age (**39.07 ± 9.42**).They showed normal neurological examination.

Methods

All electrophysiological studies were performed using Nihon Kochden electromyography machine with surface recording and stimulating electrodes. Nerve conduction studies were carried out at 33°C room temperature ***(4)***. Sensory studies were performed in all patients and controls using surface electrodes for stimulation and recording for median, ulnar and sural nerves. Motor studies were performed in all patients and controls using surface electrodes for stimulation and recording. CMAPs were recorded with surface electrodes on the abductor pollicis brevis (APB) muscle for the mediannerve, abductor digitiminimi (ADM) muscle for the ulnarnerve, extensor digitorumbrevis (EDB) muscle for the peroneal nerve, and abductor hallucis (AH) muscle for the tibial nerve***(7)***.

EMG

Standard needle EMG was performed using sterile concentric needle electrodes. For spontaneous activity assessment, analysis of the duration, amplitude and incidence of polyphasic potentials (> 4 phases) of motor unit action potentials ***(8)***.

Statistical Analysis

Statistical analysis of the present study was conducted, using the mean, standard error, correlation analysis and chi-square. All statistical analyses were performed using SPSS 19 for Windows. Results: The study included one hundred and twenty five cases of polyneuropathy**, 78 male (62.4%): 47 female (37.6%)**, who were classified according to the criteria proposed by the ESTEEM group ***(6)***.The mean age of subjects was **44.75 ± 17.66**years. Cases were divided into 36 patients with axonal polyneuropathy, 23 patients with demyelinating polyneuropathy, 9 patients with mixed polyneuropathy, while 57 patients were classified as neuropathic.

Table1. *Etiology of cases with axonal and demyelinating polyneuropathies*

	Number of cases
Axonal polyneuropathies	
Unknown	12
Diabetic neuropathy	9
Axonal GBS	7
Hereditary neuropathy	3
Uremic neuropathy	3
Vasculitic neuropathy	1
Sarcoid neuropathy	1
Total	**36**
Demyelinating polyneuropathies	
CIDP	10
Demyelinating GBS	6
Hereditary neuropathy	3
Unknown	3
MMN	1
Total	**23**

GBS, Guillain–Barre syndrome; CIDP, chronic inflammatory demyelinatingpolyneuropathy; MMN, Multifocal motor neuropathy.

Table2. *Clinical findings in patients with axonal and demyelinating polyneuropathies.*

	Axonal polyneuropathy	**Demyelinating polyneuropathy**
Age (years)	46.5 ± 17.3	42 ± 18.3
Sex (male/female)	20/16	14/9
Muscle wasting n (%) Upper limbs Lower limbs	 9 (25%) 15 (41.7%)	 6 (25%) 7 (30.4%)

Motor weakness n (%)		
Facial	9 (25%)	13 (56.5%)
Bulbar	4 (11.1%)	4 (17.4%)
Upper limbs	28 (77.8%)	21 (91.3%)
Lower limbs	36 (100%)	23 (100%)
Hypo/areflexia n (%)		
Upper limbs	24 (66.7%)	21 (91.3%)
Lower limbs	36 (100%)	23 (100%)
Distal loss/reduction of pin prick sensation n (%)		
Upper limbs	24 (66.7%)	18 (78.3%)
Lower limbs	34 (94.4%)	22 (95.7%)
loss/ reduction of vibration sense at ankles (medial malleolus) n (%)	34 (94.4%)	22 (95.7%)

Table3. *Analyzed nerve conduction studies*

	Axonal		Demyelinating	
Nerve	**Motor (n)**	**Sensory (n)**	**Motor (n)**	**Sensory (n)**
Median	16 (36/0)	11 (36/12)	19 (23/0)	10 (23/7)
Ulnar	26 (36/0)	10 (36/12)	18 (23/0)	9 (23/6)
Peroneal	24 (36/8)		13 (23/7)	
Tibial	23 (36/6)		13 (23/3)	
Sural		8 (36/25)		5 (23/16)
Total	89	29	63	24

This table showing the number of analyzed nerve segments with the total number of examined segments and the number of absent responses are indicated in parentheses.

Table4. *The correlation between reduction in SNAP amplitude and decrease in CV of sensory nerves in axonal and demyelinating polyneuropathy*

Axonal polyneuropathy		
Sensory nerves	**(r)**	**p. value**
Median nerve	0.784	0.004*
Ulnar nerve	0.849	0.002*
Sural nerve	0.270	0.518
Demyelinating polyneuropathy		
Median nerve	0.734	0.016*
Ulnar nerve	0.844	0.004*
Sural nerve	0.285	0.642

There is statistically significant linear correlation between reduction in SNAP amplitude and decrease in sensory CV of median and ulnar nerves while no significant correlation was found between reduction in SNAP amplitude and sensory CV of sural nerve in both axonal and demyelinating polyneuropathy.

Table5. *The correlation between reduction in CMAP amplitude and increase in distal motor latency of motor nerves in axonal and demyelinating polyneuropathy.*

Axonal polyneuropathy		
Motor nerves	**(r)**	**p. value**
Median nerve	- 0.761	0.001*
Ulnar nerve	- 0.612	0.001*
Peroneal nerve	- 0.677	0.000*
Tibial nerve	- 0.812	0.000*
Demyelinating polyneuropathy		
Median nerve	- 0.640	0.003*
Ulnar nerve	- 0.521	0. 027*
Peroneal nerve	- 0.300	0. 297
Tibial nerve	- 0.738	0. 002*

There is statistically significant inverse correlation between reduction in CMAP amplitude and increase in DML of median, ulnar and tibial nerves in both axonal and demyelinating

polyneuropathy, while in peroneal nerve, significant inverse correlation was found in axonal but not in demyelinating polyneuropathy.

Table6. *The correlation between reduction in CMAP amplitude and decrease in conduction velocity of motor nerves in axonal and demyelinating polyneuropathy.*

Axonal polyneuropathy		
Motor nerves	**(r)**	**p. value**
Median nerve	0.709	0. 002*
Ulnar nerve	0.605	0. 001*
Peroneal nerve	0.664	0. 000*
Tibial nerve	0.666	0. 001*
Demyelinating polyneuropathy		
Median nerve	0.637	0. 003*
Ulnar nerve	0.761	0. 000*
Peroneal nerve	0.178	0. 541
Tibial nerve	0.584	0. 036*

There is statistically significant linear correlation between reduction in CMAP amplitude and decrease in motor CV of median, ulnar, peroneal and tibial nerves in axonal polyneuropathy while in demyelinating polyneuropathy, significant linear correlation was found in median, ulnar and tibial nerves but not in peroneal nerve.

Table7. *Correlations between distal motor latency in each tested nerve and the strength of their muscular counterparts (MRC grade) in axonal and demyelinating polyneuropathy.*

Axonal polyneuropathy		
Nerve	**(r)**	**p. value**
Median nerve	0.057	0.739
Ulnar nerve	0.106	0.538
Peroneal nerve	- 0.214	0.273
Tibial nerve	- 0.087	0.647
Demyelinating polyneuropathy		
Median nerve	- 0.381	0.073
Ulnar nerve	- 0.344	0.108
Peroneal nerve	- 0.327	0.217
Tibial nerve	- 0.571	0.009*

There is no significant correlation between distal motor latency and grade of power (MRC grade) in median, ulnar and peroneal nerves while in tibial nerve in demyelinating polyneuropathy, statistically significant inverse correlation was found between prolongation of distal motor latency and decrease of grade of power.

Table8. *Correlations betweencompound muscle action potential amplitudein each tested nerve and the strength of their muscular counterparts (MRC grade)in axonal and demyelinating polyneuropathy.*

Axonal polyneuropathy		
Nerve	**(r)**	**p. value**
Median nerve	0.621	0.000*
Ulnar nerve	0.688	0.000*
Peroneal nerve	0.376	0.049*
Tibial nerve	0.513	0.004*
Demyelinating polyneuropathy		
Median nerve	0.522	0.011*
Ulnar nerve	0.436	0.038*
Peroneal nerve	0.830	0.000*
Tibial nerve	0. 830	0. 000*

There is statistically significant linear correlation between reduction in CMAP amplitude and decreased grade of power (MRC grade) in median, ulnar, peroneal and tibial nerves in both axonal and demyelinating polyneuropathy.

Table9. *Correlations between conduction velocityin each tested nerveandthe strength of their muscular counterparts (MRC grade) in axonal and demyelinating polyneuropathy.*

Axonal polyneuropathy		
Nerve	**(r)**	**p. value**
Median nerve	0.250	0.141
Ulnar nerve	0.009	0.960
Peroneal nerve	0.366	0.055
Tibial nerve	0.136	0.482
Demyelinating polyneuropathy		
Median nerve	0.304	0.158
Ulnar nerve	0.460	0.027*
Peroneal nerve	0.329	0.213
Tibial nerve	0.241	0.307

There is no significant correlation between conduction velocity and grade of power (MRC grade) in median, peroneal and tibial nerves while in ulnar nerve in demyelinating polyneuropathy, statistically significant linear correlation was found between decrease inconduction velocity and decreases in grade of power.

DISCUSSION

The results in the present study showed a linear correlation betweenamplitude reduction andconduction slowing in the majorityof motor nerves and alsosensory nerves in both groups of axonal and demyelinating polyneuropathy.

Axonal Polyneuropathies

The findings in the present study confirm the results of the study presented by ***Tankisi et al. (9)***who found the SNAP amplitude reduction to be linearly correlated with decrease in sensory CV in axonal polyneuropathy. The correlation in motor nerves for axonal polyneuropathy in the present study confirmed the mentioned study compared nerve conduction measures in axonal and demyelinating polyneuropathies.

Demyelinating Polyneuropathies

In the study presented here, a linear correlation between reductions in sensory nerve action potential amplitude and decrease in sensory conduction velocity was found in most nerves in patients with demyelinating polyneuropathies. These findings are going with that of ***Krarup and Trojaborg (10)*** who reported slowing of sensory conduction in association with markedly decreased SNAP amplitude inpatients with chronic acquired demyelinating polyneuropathy. These findings also confirm the study by ***Tankisi et al (9)*** who found the slowing of sensory conduction to be linearly correlated with reduction in SNAP amplitude in patients with demyelinating polyneuropathies of different etiologies. In motornerves, the linear correlation between CMAP amplitude reduction and conduction slowing found in the present study was in agreement with the findings in the aforementioned studies by ***Krarup and Trojaborg (10)*** and ***Tankisi et al (9)***.While Wilson and colleaguesdid not find CMAP amplitude and motor CV tobe correlated in chronic inflammatory demyelinating polyneuropathy (CIDP) ***(11)***.Correlating the degree of weakness with nerve conduction parameters in the present study aimed at assessment of electro-clinical correlations in an attempt to find the potential parameters that could represent adequate biomarkers of disease activity. The results showed significant linear correlation between reduction in CMAP amplitude of median, ulnar, peroneal and tibial, nerves and decreased grade of power (MRC grade) in their muscular counterparts in both axonal as well as demyelinating polyneuropathy. Whereas prolongation of DML correlated with decrease of grade of power only in tibial nerve and conduction velocity correlated with grade of power only in ulnar nerve in demyelinating polyneuropathy. These findings support earlier studies that found the degree of weakness to be only consistently correlated with CMAP amplitudes in chronic inflammatory demyelinating polyneuropathy ***by Rajaballya and Narasimhan, (12)***, multifocal motor neuropathy by ***Feasby et al., (13)***and in demyelinating Charcot-Marie-Tooth disease by ***Kim et al., (14).***The results of the present study as regard the relationship between muscle weakness and decreased distal CMAP amplitude and the presence of needle electromyographic findings compatible with axonal loss in demyelinating polyneuropathy, in addition to previous studies, indicate that pathogenic mechanisms leading to axonal degeneration may play an important role in the outcome of the neurological deficit in patients with demyelinating neuropathies.

Summary and Conclusions

The present study demonstrates significant correlation between amplitude reduction and conduction slowing in demyelinating as well as axonal polyneuropathy, and therefore this correlation does not seem to be useful in revealing the primary pathophysiology of a polyneuropathy in the clinical routine at present. Decrease in CV, increase in DML, increase in F-wave latency, conduction block and temporal dispersion should mainly be considered. Analysis of EMG findings in the present study showed no difference between axonal and demyelinating polyneuropathies as regard spontaneous activity assessment, interference pattern analysis or motor unit action potential analysis indicating that in the differentiation of axonal and demyelinating pathologies, the value of needle EMG may be limited. The degree of muscle weakness was found to be only consistently correlated with CMAP amplitudes but not with DML or CV suggesting that CMAP amplitude can be used as a clinically relevant biomarker of disease activity in both axonal as well as demyelinating polyneuropathy. The relationship between muscle weakness and decreased CMAP amplitude and the presence of needle electromyographic findings compatible with axonal loss in demyelinating polyneuropathy, indicate that secondary axonal degeneration may play an important role in the outcome in patients with demyelinating neuropathies.

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