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Correlation between compound muscle action potential amplitude and duration in axonal and demyelinating polyneuropathy

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HIGHLIGHTS

- More knowledge about the relation between compound muscle action potential amplitude and duration in axonal lesions and demyelination may help to reveal the pathophysiology in polyneuropathies.
- Severe decrease in amplitude in demyelinating polyneuropathies is probably due to the increase in duration secondary to temporal dispersion.
- The relationship between compound muscle action potential amplitude and duration show supplementary electrodiagnostic potential in demyelinating polyneuropathies.

ABSTRACT

Objective: To get a better understanding of pathophysiology in polyneuropathies (PNPs) by correlating compound muscle action potential (CMAP) amplitude with duration.
Methods: A total of 145 motor nerve conduction studies (MNCS) in 53 axonal and 132 MNCS in 45 demyelinating PNPs were analyzed. Peroneal and tibial MNCS were done by surface stimulation while for median and ulnar nerves near nerve or surface stimulations were used. CMAP amplitude and duration were compared in axonal and demyelination PNPs. Relationships between amplitude and duration of distally and proximally evoked CMAP were examined using regression analysis.
Results: CMAP amplitude was lower and duration was increased in all examined nerves in demyelinating PNPs than in axonal PNPs. In demyelinating PNPs, an inverse linear correlation between amplitude and duration was seen in distally and proximally evoked CMAP in all examined nerves. In axonal PNPs, there was no correlation in any of the nerves neither in distally nor in proximally evoked CMAP.
Conclusions: Distal CMAP duration and the relationship between CMAP amplitude and duration show supplementary electrodiagnostic potential in demyelinating PNPs.
Significance: More knowledge about the relation between amplitude and duration in axonal lesions and demyelination may help to reveal the pathophysiology in PNPs. Significant correlation between amplitude and duration in demyelination may suggest that the severe decrease in amplitude in demyelinating PNPs is probably due to the increase in duration secondary to temporal dispersion.

1. Introduction

In evaluation of polyneuropathy, one of the main goals of the electrophysiological examination is to identify the primary pathophysiology underlying the neuropathy as either axonal or demyelinating.

Broadly speaking, primary demyelination is indicated by reduction in conduction velocity (CV), while primary axonal loss is indicated by decrease in amplitude of the sensory nerve action potential (SNAP) or the compound muscle action potential (CMAP). However, when CMAP amplitudes are markedly reduced, it is frequently difficult to determine whether amplitude reduction is due to axonal loss or demyelination (Johnsen and Fuglsang-Frederiksen, 2000; Tankisi et al., 2007; Fuglsang-Frederiksen and Pugdahl, 2011). A large number of criteria have been established for the electrodiagnosis of primary demyelinating PNPs and some of these were developed by consensus groups (AAN, 1991; Italian GBS study group, 1996; EFNS-PNS Task Force, 2005, 2010; Tankisi et al., 2005; Koski et al., 2009). Recently, distal dispersion of the CMAP has been proposed as an adjunctive electrodiagnostic criterion for inflammatory demyelination. A limit of $\geqslant$9 ms increase in

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distal CMAP duration has been proposed in the earlier criteria (Cleland et al., 2003, 2006; Thaisetthawatkul et al., 2002; EFNS-PNS Task Force, 2005) and later the limits were graded for different nerves as median ⩾ 6.6 ms, ulnar ⩾ 6.7 ms, peroneal ⩾ 7.6 ms and tibial ⩾ 8.8 ms (Isose et al., 2009; EFNS-PNS Task Force, 2010).

We suggested in an earlier study that in demyelinating PNP the observed decrease in amplitude is due to temporal dispersion (Tankisi et al., 2007). In a nerve model study of demyelination, Caliandro et al. (2007) found that temporal dispersion and decrease in amplitude were more sensitive than conduction velocity in detection of damage. These authors suggested further studies on the relation between demyelination and temporal dispersion and decrease in amplitude of the action potential (Caliandro et al., 2008).

The present study was performed in order to get a better understanding of the relation between electrophysiological findings and pathophysiology by correlating CMAP amplitude with duration in axonal and demyelinating PNPs. Furthermore, we investigated whether the correlation between CMAP duration and CMAP amplitude can be used to differentiate axonal and demyelinating PNPs.

2. Material and methods

2.1. Material

All electrophysiological studies performed at the Department of Clinical Neurophysiology, Aarhus University Hospital, from April 2001 to December 2003 were reviewed for PNP patients examined using near-nerve needle technique. In total, 69 cases were classified as axonal PNP, 49 as demyelinating PNP, and 15 as mixed PNPs, while in 192 cases the pathophysiology could not be determined according to the criteria proposed by the ESTEEM (European Standardised Telematic tool to Evaluate Electrodiagnostic Methods) group (Tankisi et al., 2005). ESTEEM guidelines have been summarized in Table 1. For the present study, pure sensory and pure motor PNPs were excluded and only sensorimotor PNPs were selected. We wanted to look at "diffuse" neuropathies and not e.g. focal motor neuropathies and also to ensure that the patients had a PNP and not e.g. anterior horn cell disorder. Therefore we excluded motor neuropathies. A total of 53 cases of sensorimotor axonal and 45 cases of sensorimotor demyelinating PNPs were analyzed.

The possible etiologies of the selected PNPs that were diagnosed by history, clinical findings, laboratory tests and electrophysiology were published before (Tankisi et al., 2007). Most patients with axonal PNP had unknown etiology (42 out of 53). Of 45 patients with demyelinating PNP, 16 had acute inflammatory demyelinating polyradiculoneuropathy (AIDP), 16 had chronic inflammatory demyelinating PNP (CIDP) and 9 hereditary PNP. Unfortunately, the clinical severity of the PNPs could not be obtained due to the retrospective design of the study.

With distal stimulation of the nerves, a total of 145 motor nerve conduction studies (MNCS) (40 median, 27 ulnar, 34 tibial and 44 peroneal) were analyzed in 53 axonal PNPs, and 132 MNCS (44 median, 35 ulnar, 27 tibial and 25 peroneal) in 45 demyelinating PNPs. Some of the nerves were not stimulated proximally by the decision of the examining physician. A total of 134 MNCS (37 median, 19 ulnar, 34 tibial and 44 peroneal) were analyzed in 53 axonal PNPs, and 129 MNCS (44 median, 34 ulnar, 27 tibial and 24 peroneal) were analyzed in 45 demyelinating PNPs.

Table 1
ESTEEM (European Standardised Telematic tool to Evaluate Electrodiagnostic Methods) guidelines for pathophysiological classification of polyneuropathy (PNP) (Tankisi et al., 2005). CV: Conduction Velocity, DML: Distal Motor Latency, CMAP: Compound Muscle Action Potential, SNAP: Sensory Nerve Action Potential, UE: Upper Extremity, LE: Lower Extremity, ↑: increase, ↓: decrease.

1. *Demyelinating PNP:* Two nerves fulfilling definite demyelinating criteria[a] **or** one nerve fulfilling definite demyelinating criteria *and* two nerves fulfilling probable demyelinating criteria[b] **or** four nerves fulfilling probable demyelinating criteria

Criteria for definite demyelination:
- (a) >5.5 SD↓ in sensory/motor CV
- (b) >8 SD↑ in DML
- (c) >8 SD↑ in F-wave latency
- (d) Definite conduction block: CMAP amplitude decay of ⩾50% in UE or ⩾60% in LE
- (e) Increased temporal dispersion: ⩾30%↑ in negative-peak CMAP duration

Criteria for probable demyelination:
- (a) >4.5 SD – <5.5 SD↓ in sensory/motor CV
- (b) >6.0 SD – <8 SD↑ in DML
- (c) >7.0 SD – <8 SD↑ in F-wave latency
- (d) Probable conduction block: CMAP amplitude decay of ⩾40%–<50% in UE and ⩾50–<60% in LE

2. *Axonal PNP:* Two nerves fulfilling criteria for axonal loss:
Sensory nerves: ⩾2.5 SD↓ in SNAP amplitude *and* ⩽2.5 SD↓ in sensory CV
Motor nerves: ⩾2.5 SD↓ in CMAP amplitude *and* ⩽2.5 SD↓ in motor CV or ⩽2.5 SD↑ in DML *and* consistent EMG findings
3. *Mixed PNP:* Fulfilled criteria for demyelinating PNP *and* fulfilled criteria for axonal PNP in different nerves

[a] At least one of the definite demyelinating criteria a–e fulfilled in each nerve.
[b] At least one of the probable demyelinating criteria a–d fulfilled in each nerve.

2.2. Methods

CMAPs were recorded with surface electrodes in the abductor pollicis brevis (APB) muscle for the median nerve, abductor digiti minimi (ADM) muscle for the ulnar nerve, extensor digitorum brevis (EDB) muscle for the peroneal nerve, and abductor hallucis (AH) muscle for the tibial nerve. In peroneal and tibial nerves motor conduction studies were performed using surface electrodes for stimulation. In median and ulnar nerves needle electrodes in the wrist and surface electrodes in the elbow were used for stimulation. A distal distance of 65 mm for median and ulnar nerves and 90 mm for the peroneal and tibial nerves were sought to be obtained, however because of retrospective design of the study, in some cases the distal distance slightly differed. Amplitudes were measured peak-to-peak (Rosenfalck and Rosenfalck, 1975).

For the purposes of assessing the distal CMAP duration, CMAP duration was defined as the time period from onset of the first negative deflection to return to baseline of the last negative deflection and the terminal positive deflection of CMAP was not included (Thaisetthawatkul et al., 2002). When CMAP was polyphasic a total duration was calculated. The marking for duration was performed by one of the authors without knowing the clinical information at a time later than the electrophysiological examination.

In Fig. 1, distal CMAP duration was shown for different types of PNPs, (a) normal duration in a patient with axonal PNP (b) decreased duration in a patient with axonal PNP (c) prolonged duration of a CMAP with a single negative component in a patient with CIDP (d) prolonged duration of a polyphasic CMAP with multiple negative components in a patient with CIDP.

For each motor nerve, we also calculated the percentage drop in CMAP amplitude and percentage increase in the duration between proximal and distal stimulation sites to determine the presence of conduction block and temporal dispersion, respectively, in the forearm or lower leg nerve segments.

CMAP amplitude and duration were compared in axonal and demyelination PNPs with *t*-test. Relationships between the amplitude vs. the duration were examined using regression analysis for both distally and proximally evoked CMAP. Logarithmic transformation of CMAP amplitude and duration was done due to skewed data distributions. Furthermore, the correlations between the percentage increase in the duration vs. percentage decrease in the amplitude in the forearm and lower leg segments were also analyzed using regression analysis. The Statistical Packages for Social