Duration and temporal dispersion measurements in CIDP subjects from the Polyneuropathy and Treatment with Hizentra (PATH) study

D. Menon, MD[1]; J. Vijayan, MD[1];
John-Philip Lawo, MsC[2];Orell Mielke, MD[2];
M. Ngo, RT[1]; J. Dela Cruz[1]; V. Bril, MD, FRCP[1]

[1]Ellen & Martin Prosserman Centre for Neuromuscular Diseases, University Health Network, University of Toronto, Toronto, Canada
[2]CSL Behring, Marburg, Germany

ABSTRACT

Introduction: Distal compound muscle action potential (dCMAP) duration and temporal dispersion (TD) are electrophysiological hallmarks of demyelination and important for the diagnosis of CIDP. While the impact of CIDP treatment on other nerve conduction parameters has been examined, the effects on dCMAP and TD remain unexplored. The aim of the study was to examine the impact of withdrawal of immunoglobulin treatment on dCMAP duration and TD, and also the influence of the measurement technique on dCMAP duration and TD.

Methods: Nerve conduction studies were analyzed from the PATH (Polyneuropathy and Treatment with Hizentra) study which randomized patients with CIDP to two doses of IgPro 20 and placebo. Distal CMAP duration and TD were obtained by two methods of measurements (D1 and D2, TD1 and TD2) from the median and peroneal nerves.

Results: The dCMAP and TD were obtained from 480 tracings. While the two methods of measurement showed differences in D1 and D2 with D2 longer than D1 in all the three groups, there was no difference between the TD1 and TD2. There was no difference at baseline in dCMAP duration or TD among the three groups. At the end of treatment, patients in the placebo arm had no worsening of dCMAP and TD compared to baseline or the treated groups.

Conclusion: dCMAP duration and TD did not show a difference between treated and placebo groups, and may be less sensitive measures than other nerve conduction parameters when evaluating changes in treatment. The method of dCMAP duration measurement does not affect TD as long as a consistent method is followed.

Keywords: *cmap duration, temporal dispersion, chronic inflammatory demyelinating polyneuropathy*

Introduction

Nerve conduction studies form a corner stone in the diagnosis of CIDP but their role as a biomarker of treatment response has been questionable [1]. Studies have shown conflicting results in this regard but recent evidence shows nerve conduction changes can reflect the response to treatment and clinical outcome and could even be a potential marker of prognosis [2–5]. Patients with CIDP who were newly treated with IVIG had an improvement in conduction block and CMAP amplitudes and the improvement in the latter had a clear correlation with clinical outcomes [6]. In addition, deterioration of distal motor latency, conduction velocity and conduction block (CB) has been demonstrated with withdrawal of treatment leading to worsening of these conduction parameters along large nerve fibres [2]. Among the various electrophysiological features of demyelination, prolonged distal compound muscle action potential (dCMAP) duration and abnormal temporal dispersion (TD) are two hallmark features of non-uniform demyelination and are included in the EFNS/PNS guidelines for evidence of CIDP [1]. However, unlike other nerve conduction parameters in CIDP, changes in these parameters in response to treatment have not been explored. Measurement of dCAMP duration, and from it TD, are not as straightforward as are other NCS measures, and different methods have been used over the years to calculate CMAP duration. The measurement of TD is less ambiguous but dependent on CMAP duration and is the percentage increase between proximal and distal CMAP duration, with more than 30% considered abnormal [1]. The current study examines the impact of withdrawal of immunoglobulin treatment on dCMAP duration and TD, and also the influence of different methods of measurement of dCMAP duration and thus, temporal dispersion.

Methods

The nerve conduction data analyzed in this study are obtained from the PATH study, the protocol of which has been described in detail previously [2,7]. As a brief overview, subjects with CIDP who were IVIG-dependent were randomized to receive 0.2 g/kg (low dose) and 0.4 g/kg (high dose) body weight weekly doses of SCIG (IgPro20 [Hizentra®]; CSL Behring, King of Prussia, PA, USA) or placebo (albumin). 57 subjects were assigned to 0.2 g/kg bodyweight IgPro20, 58 subjects to 0.4 g/kg body weight IgPro20 and 57 subjects were assigned to placebo. The nerve conduction studies (NCS) were performed at the start and end of the subcutaneous treatment interval at the Week 25 visit. A core lab monitored all procedures and approved all tracings for compliance with protocol. This included first

testing healthy volunteers to use as controls and ensuring all waveforms were reviewed by the core lab to validate the data against the controls. Two motor nerves: median in the upper limb and peroneal in the lower limb were measured according to standards of the AANEM/CSCN. The stimulation sites were at the elbow and wrist for the median nerve and lateral popliteal fossa, below the fibular head and ankle for the peroneal nerves. All studies were done with surface stimulating and recording electrodes, under careful temperature controls so that the upper limb temperature was maintained at ≥ 32°C and the lower limb at ≥ 31°C. We randomly selected the tracings of 20 subjects from each group for the current study. The parameters assessed in the current study included distal CMAP (dCMAP) duration and temporal dispersion (TD) which we measured as per the AANEM guidelines as well as the European Federation of Neurological Societies/Peripheral Nerve Societies (EFNS/PNS) 2010 electrodiagnostic criteria for CIDP. Accordingly, we measured dCMAP duration (D1) by measuring the duration from the onset of first negative peak to first baseline crossing and used these measurements to obtain TD1 [8]. We also calculated dCMAP and TD as per the definitions of EFNS/PNS 2010 electrodiagnostic criteria for CIDP whereby we measured dCMAP duration (D2) from onset of first negative peak to return to baseline of last negative peak and from it, TD (TD2). TD was measured as percentage duration increase of the proximal from the distal negative peak of CMAP, with more than or equal to 30% being abnormal (Figure 1) [1]. Each tracing from median and peroneal nerves from the wrist and elbow, ankle and fibular head, respectively, was analyzed from the tracings obtained at the beginning and at the end of treatment and dCMAP duration (D1 and D2) and TD (TD1 and TD) were calculated. We excluded those tracings if the CMAP amplitude was less than 20% of normal or inelicitable (12 in high dose, 36 in low dose and 8 in placebo). Subsequent analysis was done independently for both measurements by comparing the dCMAP duration (D1 and D2) and TD (TD1 and TD2) for peroneal and median nerves at the start and at the end of the treatment for the three treatment groups.

Analysis was done using SPSS version 20, IBM® Armonk, New York. The dCMAP duration and TD for the three groups are expressed as means with standard deviation. Box whisker plots are used to represent the TD (TD1 and TD2) and dCMAP duration (D1 and D2) at baseline and last visit for high dose, low dose and placebo groups. The tests of normality confirmed the non-normal distribution of data and non-parametric tests were used to compare the TD and dCMAP durations at baseline and final visit (Wilcoxon signed rank test) and also to compare between the two measurements methods, for the three treatment groups (D1 vs D2; TD1 vs TD2; Mann Whitney U test), and between treatments at baseline (Kruskal-Wallis test).

Results of these exploratory analyses were not adjusted for multiplicity and were considered statistically significant if $p < 0.05$.

Results

A total of 480 tracings from median and peroneal nerves were reviewed from the high dose SCIG, low dose SCIG and placebo groups and 424 tracings were included for analysis. The mean dCMAP duration in milliseconds and the mean TD in percentage prolongation by both methods at baseline and at end of treatment are shown in table 1, figures 1 and 2. At baseline, there was no difference in the dCMAP duration or temporal dispersion among the three groups with either measurement method (Table 2). A significant difference was found between baseline dCMAP durations calculated by the two measurement methods (D1 vs D2) with mean dCMAP duration longer for D2 than D1. However, there was no difference in the TD at baseline with either method (Table 3). The results were the same for comparisons at the end of the treatment intervals as well (Table 4).

Lastly, comparison was made between the corresponding parameters at baseline and end of treatment to determine if withdrawal of treatment produced any change. There was no significant difference in any of the parameters, using either method of measurement, for dCMAP or TD at baseline or at end of the treatment (Table 5). A separate analysis combining the two treatment arms as compared with the placebo group also did not reveal any significant difference (Table 6). We performed the analysis separately for median and peroneal nerve parameters for

Table 1: Baseline and final dCMAP duration (D1 and D2) and TD (TD1 and TD2) for high dose, low dose and placebo groups

Measurement	N	Mean ± standard deviation
High dose baseline D1†	35	6.4 ± 1.5
High dose final D1	35	6.4 ± 2.2
High dose baseline D2	35	10.4 ± 3.8
High dose final D2	35	11.4 ± 4.1
High dose baseline TD1‡	33	18.9 ± 21.3
High dose final TD1	33	19.5 ± 21.8
High dose baseline TD2	34	22.2 ± 32.6
High dose final TD2	34	18.7 ± 25.4
Low dose baseline D1†	32	6.9 ± 2.5
Low dose final D1	32	6.5 ± 3.1
Low dose baseline D2	31	11.8 ± 5.1
Low dose final D2	31	11.7 ± 5.6
Low dose baseline TD1‡	24	19.0 ± 21.9
Low dose final TD1	24	18.1 ± 24.5
Low dose baseline TD2	24	29.1 ± 54.9
Low dose final TD2	24	22.6 ± 46.2
Placebo baseline D1†	36	6.7 ± 2.1
Placebo final D1	36	6.8 ± 2.2
Placebo baseline D2	36	12.6 ± 4.7
Placebo final D2	36	13.7 ± 9.7
Placebo baseline TD1‡	35	14.7 ± 15.4
Placebo final TD1	35	17.9 ± 19.2
Placebo baseline TD2	34	17.4 ± 19.8
Placebo final TD2	34	22.2 ± 32.8

† in milliseconds, ‡ percentage prolongation

Table 2: Comparison of the baseline variables

Measurement (n)	Mean ± standard deviation	P*
High dose baseline D1† (35)	6.4 ± 1.5	0.687
Low dose baseline D1 (32)	6.9 ± 2.6	
Placebo baseline D1 (36)	6.8 ± 2.2	
High dose baseline TD1‡ (33)	19.6 ± 21.9	0.763
Low dose baseline TD1 (24)	19.0 ± 21.9	
Placebo baseline TD1 (35)	14.8 ± 15.5	
High dose baseline D2† (35)	10.4 ± 3.8	0.684
Low dose baseline D2 (31)	11.9 ± 5.1	
Placebo baseline D2 (36)	12.7 ± 4.7	
High dose baseline TD 2‡ (34)	22.4 ± 32.7	0.833
Low dose baseline TD2 (24)	29.2 ± 54.9	
Placebo baseline TD2 (34)	17.5 ± 19.8	

*Kruskal Wallis test, † in milliseconds, ‡ percentage prolongation

Table 3: Comparison of the dCMAP duration and TD calculated at baseline

Measurement by two methods	Mean ± standard deviation	P*
High dose baseline D1† (35)	6.4 ± 1.5	<0.0001
High dose baseline D2 (35)	10.4 ± 3.8	
High dose baseline TD1‡ (33)	18.9 ± 21.3	0.712
High dose baseline TD2 (34)	22.4 ± 32.7	
Low dose baseline D1† (32)	6.9 ± 2.6	<0.0001
Low dose baseline D2 (31)	11.9 ± 5.1	
Low dose baseline TD1‡ (24)	19.0 ± 21.9	0.895
Low dose baseline TD2 (24)	22.7 ± 46.3	
Placebo baseline D1† (36)	6.7 ± 2.1	<0.0001
Placebo baseline D2 (36)	12.7 ± 4.7	
Placebo baseline TD1‡ (35)	14.8 ± 15.5	0.772
Placebo baseline TD2 (34)	17.5 ± 19.8	

*Mann Whitney U test, † in milliseconds, ‡ percentage prolongation

Table 4: Comparison of the variables at end of treatment

Measurement (n)	Mean ± standard deviation	P*
High dose final D1† (35)	6.4 ± 2.1	0.773
Low dose final D1 (32)	6.6 ± 3.1	
Placebo final D1 (36)	6.7 ± 2.1	
High dose final TD1‡ (33)	18.9 ± 21.3	0.893
Low dose final TD1 (24)	18.2 ± 24.6	
Placebo final TD1 (35)	17.9 ± 19.2	
High dose final D2† (35)	11.4 ± 4.1	0.664
Low dose final D2 (31)	11.7 ± 5.6	
Placebo final D2 (36)	13.7 ± 9.8	
High dose final TD2‡ (34)	18.7 ± 25.5	0.876
Low dose final TD2 (24)	22.7 ± 46.3	
Placebo final TD2 (34)	22.2 ± 32.9	

*Kruskal Wallis test

Table 5: Comparison between the baseline and final dCMAP duration and TD before and after the high dose, low dose and placebo groups

Comparison of means	Mean difference‡ ± standard deviation	95% confidence interval of difference		P*
		Lower limit	Upper limit	
High dose baseline D1 vs High dose final D1	0.02 ± 1.6	-.55	.58	0.586
High dose baseline D2 vs High dose final D2	-0.96 ± 3.3	-2.1	.17	0.051
High dose baseline TD1 vs High dose final TD1	-0.6 ± 22.6	-8.6	7.4	0.787
High dose baseline TD2 vs High dose final TD2	3.4 ± 30.1	-7.1	13.9	0.318
Low dose baseline D1 vs Low dose final D1	0.35 ± 2.8	-.65	1.34	0.713
Low dose baseline D2 vs Low dose final D2	0.17 ± 5.5	-1.8	2.2	0.263
Low dose baseline TD1 vs Low dose final TD1	0.85 ± 12.9	-4.6	6.3	0.823
Low dose baseline TD2 vs Low dose final TD2	6.5 ± 60.8	-19.2	32.2	0.263
Placebo baseline D1 vs Placebo final D1	-0.12 ± 0.81	-0.39	0.16	0.451
Placebo baseline D2 vs Placebo final D2	-1.1 ± 10.8	-4.8	2.5	0.819
Placebo baseline TD1 vs Placebo final TD1	-3.2 ± 18.9	-9.7	3.3	0.330
Placebo baseline TD2 vs Placebo final TD2	-4.7 ± 33.9	-16.5	7.1	0.971

*Wilcoxon singed rank test

Table 6: Comparison of variables between the treatment (low dose and high dose SCIG combined) with placebo arm

Measurement (n)	Mean ± standard deviation	P*
Treated baseline D1 (67)	6.6 ± 2.1	0.885
Placebo baseline D1 (36)	6.7 ± 2.1	
Treated baseline D2 (66)	11.1 ± 4.5	0.175
Placebo baseline D2 (36)	12.6 ± 4.8	
Treated baseline TD1 (52)	19.8 ± 22.2	0.463
Placebo baseline TD1 (35)	14.7 ± 15.4	
Treated baseline TD2 (58)	24.5 ± 41.1	0.836
Placebo baseline TD2 (34)	18.2 ± 9.9	
Treated final D1 (67)	6.5 ± 2.6	0.562
Placebo final D1 (36)	6.7 ± 2.3	
Treated final D2 (66)	11.6 ± 4.8	0.462
Placebo final D2 (36)	13.6 ± 9.7	
Treated final TD1 (57)	19.5 ± 22.7	0.753
Placebo final TD1 (35)	19.7 ± 19.6	
Treated final TD2 (58)	22.5 ± 37.5	0.681
Placebo final TD2 (34)	22.3 ± 32.4	

*Mann Whitney U test

the three groups, with the same results.

Discussion

The current study did not find any difference in dCMAP duration or TD, between the baseline and at the end of the treatment, in patients with CIDP withdrawn from immunoglobulin treatment. There was no worsening in these parameters in patients treated with placebo compared to those remaining on treatment with subcutaneous immunoglobulin. We employed two methods of measurement for dCMAP duration and TD, and while these methods demonstrated a significant difference in dCMAP durations, there was no difference in the calculated TDs with either method. dCMAP duration and TD did not change on withdrawal of immunoglobulin treatment despite the method in which these parameters were measured. The measurements showed high variability, and since only small changes are expected in this short duration study, it may be that the measures lack sufficient precision to show change.

Prolonged distal CMAP duration and temporal dispersion are markers of demyelination and are used in the electrophysiological diagnosis of CIDP [1]. Although conventionally most authorities prefer measuring CMAP duration from the initial negative deflection to first return to baseline, in CIDP it is recommended that the CMAP duration be measured from the onset of the first negative deflection to return to baseline of the last negative deflection to baseline [1,9–12]. Some authorities have also

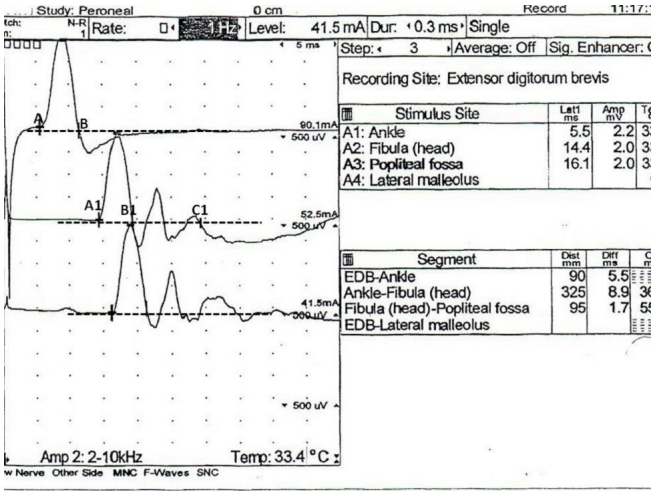

Figure 1: Caption: Representative nerve conduction study from peroneal nerve showing the measurement of duration 1 (D1) and duration 2 (D2) and corresponding temporal dispersions (TD1 and TD2)

Legend: In A1 tracing the distal CMAP (dCMAP) duration D1 was measured as interval between A and B in milliseconds. Here, since point B is the return to baseline of the only negative peak, D1 will be equal to D2. In tracing A2, proximal D1 will be equal to interval between A1 and B1 and proximal D2 will be equal to interval between A1 and C1, the latter being the return to baseline of the last negative peak. Temporal dispersion is then calculated as the percentage prolongation of proximal D1 to distal D1 and proximal D2 to distal D2, which respectively gives TD1 and TD2.

compared the negative peak duration with total duration of CMAP and found slight advantages favoring each method, but measuring the negative peak duration is less technically demanding [13,14]. Practically, the return to baseline of the last negative peak, especially in a multiphasic CMAP (Figure 1, tracing A3), is not easy to identify and even minor differences in cursor placement alter the results of the duration value and therefore the TD2, as this relies on comparison of the distal to proximal CMAP duration. It has been speculated that measurement of CMAP duration by either method is acceptable with the use of additional qualifiers such as multiple turns or a multiphasic CMAP to provide further clarity [15]. Our findings demonstrate that while there are obvious differences in the dCMAP duration measurements obtained with the two methods, the calculated TD does not vary as long as the method is consistent for measuring distal and proximal CMAP durations.

The positive impact of immunoglobulins in treatment of CIDP is well recognized. However, the mechanism by which immunoglobulins bring about rapid improvement is unclear and is unlikely to be due to remyelination or axonal regeneration. Nerve excitability studies showed rapid changes post-IVIG preceding clinical and routine nerve conduction changes in CIDP and might be due to restoration of persistent inward sodium currents and membrane properties [16–18]. Several nerve conduction parameters of demyelination, including distal motor latency, conduction velocity, CMAP amplitude and conduction block (CB), showed changes with immunoglobulins or withdrawal of this therapy [2,3,19,5]. Definite correlations with clinical improvement have been shown in some studies and not others, although the largest study to date did show such correlations [2,3,5,20–22]. Additional evidence of the treatment responsiveness of NCS is given by the fact that patients who were initially responsive to IVIG had worsening in distal motor latency and conduction velocity when switched to placebo, but at the same time, patients who continued to receive immunoglobulins remained stable [2]. Despite being important markers of demyelination, dCMAP duration and TD have not received wide attention in the setting of CIDP, perhaps due to a lack of a physiological correlates, unlike CMAP amplitudes and CB. But these parameters do have electrophysiological importance, and abnormal TD precludes a diagnosis of CB [11]. Besides, TD has been found to improve significantly in multifocal motor neuropathy with conduction block with treatment and is perhaps a more sensitive marker of improvement than other NCS parameters in this disorder [23]. Thus intuitively, both CMAP duration and its derivative TD would be expected to change with treatment in CIDP. However, our study did not show any difference at the end of 24 weeks for the placebo arm when treatment was withdrawn. This may be because the duration of treatment withdrawal was too short at 6 months, although other NCS parameters such as conduction velocity did change [2]. Another reason might be that these various measures that are thought to show 'demyelination' have different underlying pathophysiological mechanisms. CMAP duration and temporal dispersion are thought to be classical features of acquired demyelination manifesting due to diffuse differential slowing of conduction along nerve fibers and the resulting asynchrony of the CMAP. On the other hand, CB is focal and experimental studies show that CB can start within an hour of an inciting event, well before any structural changes of demyelination set in [24]. This may be due to paranodal disruption of ion channels which is more amenable to rapid reversal with immunoglobulins, while in contrast, features such as temporal dispersion and prolonged duration may be due to structural demyelination and thus take longer to recover or manifest [18]. In addition, the associated secondary axonal changes also would invariably color the nerve conduction findings and is recognized as one of the reasons for poor response to IVIG. In a case of CIDP, the actual electrophysiological picture would thus be the net effect of all these differing pathophysiological mechanisms, each of which may respond differently to treatment or withdrawal of treatment. The duration of the disease and follow-up may also have an impact on the nerve conduction findings which can evolve more rapidly in the short term, when disease duration is shorter, and more slowly with longer disease duration. The precision of the different electrophysiological measures will also influence the observed changes.

Our study has a few limitations. Having focused purely on the electrophysiological parameters, this study lacks information on the clinical characteristics and treatment responsiveness. Data on the full cohort in each treatment arm was not obtained so that the results may have differed with a larger sample size. Even though the study analyzed a large number of nerve tracings in patients with CIDP, the actual number of nerve conduction studies with abnormal dCMAP duration and TD was relatively low which also would impact the generalizability, although all patients in this study fulfilled EFNS/PNS criteria for CIDP. This suggests a low sensitivity of duration and TD in CIDP.

Conclusion

The current study found that dCMAP duration and TD did not differ between the treated and placebo arms in patients with CIDP. These results suggest that duration and TD are less sensitive to withdrawal of treatment than other NCS parameters such as motor latencies and conduction

velocities that changed as immunoglobulin therapy was removed. While the exact method of measuring dCMAP duration has been a topic of debate, the method does not have a bearing on TD as long as consistency in method is followed and this is relevant for routine practice. Further studies are needed to look at the correlation between dCMAP and TD with other electrophysiological parameters and patient outcomes.

Corresponding Author
Vera Bril, 5EC-309, Toronto General Hospital,
200 Elizabeth St, Toronto, ON, Canada, M5A 4H9
Vera.bril@utoronto.ca
Phone: 1-416-340-3315
Fax: 1-416-340-4189

References

[1] Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society - First Revision. Journal of the Peripheral Nervous System 2010;15:1–9. https://doi.org/10.1111/j.1529-8027.2010.00245.x.

[2] Bril V, Hartung H-P, Lawo J-P, Durn BL, Mielke O. Electrophysiological testing in chronic inflammatory demyelinating polyneuropathy patients treated with subcutaneous immunoglobulin: The Polyneuropathy And Treatment with Hizentra (PATH) study. Clinical Neurophysiology 2020. https://doi.org/10.1016/j.clinph.2020.09.001.

[3] Bril V, Katzberg H, Donofrio P, Banach M, Dalakas MC, Deng C, et al. Electrophysiology in chronic inflammatory demyelinating polyneuropathy with IGIV. Muscle Nerve 2009;39:448–55. https://doi.org/10.1002/mus.21236.

[4] Chin RL, Deng C, Bril V, Hartung H-P, Merkies ISJ, Donofrio PD, et al. Follow-up nerve conduction studies in CIDP after treatment with IGIV-C: Comparison of patients with and without subsequent relapse. Muscle Nerve 2015;52:498–502. https://doi.org/10.1002/mus.24624.

[5] Ellrichmann G, Gold R, Ayzenberg I, Yoon M-S, Schneider-Gold C. Two years' long-term follow up in chronic inflammatory demyelinating polyradiculoneuropathy: efficacy of intravenous immunoglobulin treatment. Ther Adv Neurol Disord 2017;10:91–101. https://doi.org/10.1177/1756285616679369.

[6] Bril V, Banach M, Dalakas MC, Deng C, Donofrio P, Hanna K, et al. Electrophysiologic correlations with clinical outcomes in CIDP. Muscle & Nerve 2010;42:492–7. https://doi.org/10.1002/mus.21733.

[7] van Schaik IN, Bril V, van Geloven N, Hartung H-P, Lewis RA, Sobue G, et al. Subcutaneous immunoglobulin for maintenance treatment in chronic inflammatory demyelinating polyneuropathy (PATH): a randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet Neurology 2018;17:35–46. https://doi.org/10.1016/S1474-4422(17)30378-2.

[8] guidelineConsensusCriteria.pdf n.d.

[9] Preston DC, Shapiro BE. 3 - Basic Nerve Conduction Studies. In: Preston DC, Shapiro BE, editors. Electromyography and Neuromuscular Disorders (Third Edition), London: W.B. Saunders; 2013, p. 19–35. https://doi.org/10.1016/B978-1-4557-2672-1.00003-9.

[10] Thaisetthawatkul P, Logigian EL, Herrmann DN. Dispersion of the distal compound muscle action potential as a diagnostic criterion for chronic inflammatory demyelinating polyneuropathy. Neurology 2002;59:1526–32. https://doi.org/10.1212/01.WNL.0000034172.47882.20.

[11] guidelineConsensusCriteria.pdf n.d.

[12] Ferrante MA, Bs TS, Tsao BE. Principles of Nerve Conduction Studies and Needle EMG n.d.:35.

[13] Oh SJ, Kim DE, Kuruoglu HR. What is the best diagnostic index of conduction block and temporal dispersion? Muscle & Nerve 1994;17:489–93. https://doi.org/10.1002/mus.880170504.

[14] Lagarde J, Viala K, Fournier E. Is total duration of distal compound muscle action potential better than negative peak duration in the diagnosis of chronic inflammatory demyelinating polyneuropathy? Muscle Nerve 2014;49:895–9. https://doi.org/10.1002/mus.24080.

[15] Sander HW, Oh SJ. Temporal Dispersion Terminology: Multiphasic and Multiturn CMAPs. Journal of Clinical Neuromuscular Disease 2006;7:173–4. https://doi.org/10.1097/01.cnd.0000203642.77005.27.

[16] Boërio D, Créange A, Hogrel J-Y, Guéguen A, Bertrand D, Lefaucheur J-P. Nerve excitability changes after intravenous immunoglobulin infusions in multifocal motor neuropathy and chronic inflammatory demyelinating neuropathy. J Neurol Sci 2010;292:63–71. https://doi.org/10.1016/j.jns.2010.02.002.

[17] Lin CS-Y, Krishnan AV, Park SB, Kiernan MC. Modulatory effects on axonal function after intravenous immunoglobulin therapy in chronic inflammatory demyelinating polyneuropathy. Arch Neurol 2011;68:862–9. https://doi.org/10.1001/archneurol.2011.137.

[18] Berger M, McCallus DE, Lin CS-Y. Rapid and reversible responses to IVIG in autoimmune neuromuscular

diseases suggest mechanisms of action involving competition with functionally important autoantibodies. Journal of the Peripheral Nervous System 2013;18:275–96. https://doi.org/10.1111/jns5.12048.

[19] Iijima M, Yamamoto M, Hirayama M, Tanaka F, Katsuno M, Mori K, et al. Clinical and electrophysiologic correlates of IVIg responsiveness in CIDP. Neurology 2005;64:1471–5. https://doi.org/10.1212/01.WNL.0000158680.89323.F8.

[20] Khoo A, Frasca J, Schultz D. Measuring disease activity and predicting response to intravenous immunoglobulin in chronic inflammatory demyelinating polyneuropathy. Biomark Res 2019;7. https://doi.org/10.1186/s40364-019-0154-2.

[21] Harbo T, Andersen H, Jakobsen J. Acute motor response following a single IVIG treatment course in chronic inflammatory demyelinating polyneuropathy. Muscle Nerve 2009;39:439–47. https://doi.org/10.1002/mus.21305.

[22] Khomand P, Katzberg H, Ngo M, Bril V. Electrophysiological Responsiveness to Long-Term Therapy in Chronic Inflammatory Demyelinating Polyneuropathy: Case Report. CRN 2020;12:40–4. https://doi.org/10.1159/000505234.

[23] Ghosh A, Virgincar A, Kennett R, Busby M, Donaghy M. The effect of treatment upon temporal dispersion in IvIg responsive multifocal motor neuropathy. J Neurol Neurosurg Psychiatry 2005;76:1269–72. https://doi.org/10.1136/jnnp.2004.050252.

[24] Lafontaine S, Rasminsky M, Saida T, Sumner AJ. Conduction block in rat myelinated fibres following acute exposure to antigalactocerebroside serum. J Physiol 1982;323:287–306.