Compliance with international guidelines for chronic inflammatory neuropathies

See paper by Rosier et al. on page 575.

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Management guidelines for rare diseases are produced with the primary aim of improving practice and standards of care for patients and may represent a useful framework for clinical practice. The European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) guidelines for chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN) were last published in 2010 [1,2]. However, the enthusiasm of the audience for which they are produced, arguably primarily non-subspecialists, is largely unexplored. Compliance with these guidelines by neuromuscular and/or peripheral nerve specialists has not been investigated.

In this issue of *European Journal of Neurology*, Rosier *et al*. [3] describe the findings of their study specifically in relation to intravenous immunoglobulin treatment for these disorders. They aimed, through a survey, to evaluate French daily neurological practice in relation to the above-mentioned published guidelines. They performed a retrospective observational study based on a pilot questionnaire validated by expert neurologists in the field. A total of 411 neurologists were invited by e-mail to complete a general questionnaire and four patient case reports concerning subjects who were recently seen or soon to be seen. Of the 70 responders, 49 met pre-defined criteria for inclusion in the analysis. A minority (26.6%) worked in neuromuscular reference centres (NRCs), coming from most (10/13) of the French NRCs, thereby offering an adequate global view of subspecialist practice. The authors mainly ascertained that initial treatment procedures for both CIDP and MMN conformed with existing guidelines. However, in greater detail, this essentially concerns the dose of 2 g/kg used over 5 days (the 4-weekly administration frequency with dose maintenance for the first three courses). In contrast, in relation to longer term therapy and guideline recommendations, some major and interesting discrepancies were observed, notably with non-NRC neurologists decreasing the dose of intravenous immunoglobulin significantly more frequently than NRC neurologists (83% vs. 51%; $P < 0.05$) and using immunosuppressants significantly less frequently (39% vs. 92%; $P < 0.05$). Immunosuppressants were used for nearly 40% of cases by neurologists and, although the details are not provided, it is likely that this practice was more common in NRCs. Dose reductions are recommended in the guidelines and implementation of this, according to the reported findings of Rosier *et al*. [3], appears to be less widespread amongst subspecialists. One may argue that NRCs see more severely affected subjects, although it is somewhat mystifying how this may justify sustained high-dose therapy, presumably in circumstances of stability or progressive and possibly treatment-unrelated improvement, for over one quarter of subspecialists for the first 12 treatment courses. This is compounded by the two-fold and four-fold higher follow-up frequencies of patients with CIDP and MMN, respectively, in NRCs compared with the general neurology setting, which one would have expected to make dose reduction decisions easier. However, the use of immunosuppressants, for which there is no current evidence base, is not recommended by the existing guidelines either for CIDP MMN. Despite this lack of justification, subspecialists appear to widely diverge from the recommendations in their practice, compared with generalists. However, it is also of note, and with regards to published data on the usually fixed frequency requirements particularly in CIDP [4,5], that all neurologists altered the treatment interval more frequently than dose (97% vs. 65% for CIDP and 98% vs. 51% for MMN).

These findings in themselves therefore clearly suggest poor longer-term compliance with the guidelines, which importantly, but also perplexingly, appears to predominate in NRCs. That nearly one third of patients with CIDP and nearly half of those with MMN were referred by general neurologists to NRCs suggests that cases managed by subspecialists do not differ greatly in presentation or progression from those whose treatment remained in the hands of general neurologists. It is clear, however, that subsequent patient management differs significantly within as compared with outside NRCs, which in itself, irrespective of hypothetical underlying reasons, is inconsistent with the aim and objectives of guideline generation and dissemination.

Our group conducted an international web-based audit on compliance with EFNS/PNS guidelines on CIDP and MMN between 2012 and 2015 in a total of nine countries: Italy, Belgium, Serbia, Moldova, France, Hungary, Portugal, the UK and the state of Kerala in India. The main finding of our audit was the low response rate (4.2% of all contacted potential participants globally). Nearly 60% of

non-neuromuscular neurologists stated that they used EFNS/PNS guidelines to establish their therapeutic decision-making for CIDP and MMN. However, nearly one sixth had no knowledge of the guidelines, the electrophysiological features being less commonly known than the clinical aspects, as expected. A large majority of neuromuscular neurologists preferred using EFNS/PNS criteria in clinical practice than any other criteria. Intravenous immunoglobulin dose reduction trials were, in contrast to the findings of Rosier *et al.* [3], reported as common practice for the majority of neuromuscular neurologists for long-term patients. Although in lower proportions as compared with the French study, over 50% of neuromuscular neurologists declared feeling that immunosuppression may be justified in CIDP, irrespective of the response to steroids, immunoglobulins or plasma exchange.

Our analysis, through the poor responder rate from a large, similarly sampled, e-mail-invited international neurological cohort, demonstrates a low level of interest in guidelines for rare diseases such as CIDP and MMN, particularly amongst general neurologists. Furthermore, a selection bias is likely to have occurred, as illustrated by the contrasting high level of guideline awareness in the surveyed sample. A similar selection bias is also likely in the study of Rosier *et al.* [3]. Our results indicate that the surveyed sample was aware of the guidelines but, similarly to the French cohort, behaved variably in relation to the recommendations within them.

Current EFNS/PNS guidelines represent very useful research tools as we have shown in a previous analysis [6]. However, awareness of and compliance with these guidelines appear, both from the data from Rosier *et al.* [3] and from our international analysis, much more doubtful. In the French study, the poor long-term compliance amongst NRC neurologists enhances the concerns, indicating the need for greater coherence in the subspecialist arena, so as to improve newer versions and updates for all practitioners. New guidelines will be necessarily and rightly focused on the evidence base [7,8]. However, consideration of factors impacting on dissemination and uptake will equally require careful consideration. It is hoped that this will ultimately allow the improvement and harmonization of standards of care of all affected patients.

Disclosure of conflicts of interest

The authors declare no financial or other conflicts of interest.

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**Details of the members of the European Study Group on Guidelines for Neuropathy are listed in Appendix and Appendix S1.*

Appendix

European Study Group of Guidelines for Neuropathy members: Adrian Fowle, Jean-Marc Leger, Eduardo Nobile-Orazio, Antonino Uncini, Pieter van Doorn

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Affiliations of the members of the European Study Group on Guidelines for Neuropathy.

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