Commentary

Electrodiagnostic testing in diabetic neuropathy: Which limb?

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A B S T R A C T

Electrodiagnosis of subclinical diabetic neuropathies by nerve conduction studies remains challenging. The question arises about which nerves should be tested and what the best electrodiagnostic protocol to make an early diagnosis of diabetic neuropathies would be.

On the basis of our findings and other evidence, which highlighted the remarkable prevalence of electrophysiological abnormalities in nerve conduction studies of the upper limbs, often in the presence of normal lower limb conduction parameters, we suggest that both ulnar and median nerves, in their motor and sensitive component, should be the two target nerves for electrodiagnostic protocols in diabetic neuropathies.

Overwhelming evidence has demonstrated that neuropathy is a common complication of diabetes mellitus (DM) and is burdened by impaired quality of life [1]. Peripheral nerve involvement in DM shows such a wide clinical spectrum, that the Toronto Diabetic Neuropathy Expert Group [1] considered the definition of “neuropathies” more appropriate than “neuropathy” to encompass its manifold clinical subtypes, that range from the generalized forms to the more focal ones [2].

Currently, electrodiagnosis of subclinical diabetic polyneuropathies by nerve conduction studies remains challenging. Although the ideal criteria should include some attributes representative of the most frequently observed neurophysiological abnormalities, if it is to be sensitive, there must be no excess, so as to avoid the type I error of a high false positive rate. The diagnostic criterion based on the presence of ≥1 abnormal attributes in ≥2 nerves (using the ≤5th/≥95th percentile cut-off) seems to balance sensitivity and specificity satisfactorily [2]. Establishing which nerves we should test, would enable the set-up of the best electrodiagnostic protocol to make an early diagnosis of subclinical diabetic neuropathies.

The most common generalized polyneuropathy is diabetic sensori-motor polyneuropathy, which is known to be length-dependent. Therefore, most clinicians are prone to test the nerves in the lower limbs rather than those in the upper limbs.
However, it is common place to find a normal sural sensory nerve action potential (SNAP) in patients that have abnormal results when upper limb sensory nerve conduction studies are carried out. Indeed, this was observed in a previous study of ours [3] on a sample of newly diagnosed patients with Type 2 DM, where the SNAP amplitude was below the lower threshold limit in 70% for the median nerve, 69% for the ulnar and only in 22% for the sural nerve. Moreover, in the presence of decreased SNAP amplitude of the ulnar or median nerve, the SNAP amplitude of the sural nerve was normal in 82% and 80% of the subjects respectively [3]. Such a dissociation between upper and lower limb sensory nerve involvement in DM was confirmed by another study of ours on subjects affected by Type 2 DM, where the SNAP amplitude was below the lower threshold limit in 52% of the total sample for the ulnar nerve (at the 5th finger), in 48% for the median and in 29% for the sural nerve [4]. The SNAP amplitude of the sural nerve was normal, in the presence of a decrease in the SNAP amplitude of the ulnar nerve (pattern “abnormal ulnar/normal sural”) in 34% of the subjects. These findings may be only partially explained by the high prevalence of the carpal tunnel syndrome and ulnar nerve entrapments, which were diagnosed in these two studies [3,4] and, more generally, in patients with DM [5]. Indeed, a median mononeuropathy at the wrist was found in 28% and 62.5% of the two patient samples respectively, the former with DM at diagnosis, the latter with an average disease duration of 14.5 years [3,4]. Furthermore, subclinical ulnar entrapments were electro-diagnosed at the elbow in 34% of the patients and in 11% at the wrist [4], suggesting that the ulnar nerve is very susceptible to focal entrapment in DM, similarly to the median nerve. This is most likely due to the metabolic factors and endoneurial ischemia that occur in DM in the long preclinical stage [6] as they damage the nerve, making it more susceptible to focal entrapment at an early stage, where the focal neuropathy of the median [7] or ulnar nerve [3] may be the only manifestation of a peripheral nerve involvement.

However, such a peculiar pattern of “abnormal median or ulnar/normal sural” was detected even in the absence of entrapments of the ulnar nerve in about 50% of the subjects in the aforementioned studies [3,4], although carried out on relatively small samples of DM patients (56 and 64 respectively). Similarly, in a recent study [8] on a larger sample of 500 patients affected by diabetic neuropathies at an early stage, the SNAP amplitude turned out to be the most sensitive neuropathy marker, in agreement with previous findings by Bi et al. [9]. The highest rate of abnormality was observed in the median nerve SNAP (42.3%), followed by alterations in that of the ulnar (36.6%) [8].

In a previous study [10], the pattern of an “abnormal median-normal sural” sensory response was detected in a large number of patients with acute inflammatory polyneuropathy and was interpreted as an electrophysiological marker of an early distal nerve involvement. This seems to be also in agreement with the well-known dying-back pathophysiological mechanisms underlying generalized typical, symmetrical, length-dependent diabetic neuropathy, where the metabolic derangement and microvessel alterations, subsequent to chronic hyperglycemia, lead to exhaustion of the ATP supply and to an earlier fiber dissolution in the distal nerve compartment [11].

This hypothesis may well explain the more frequent finding of abnormality in the upper limb sensory nerve conduction studies in our patients with DM at diagnosis, as the early sign of distal sensory fiber involvement. Indeed, the routine sensory median or ulnar nerve conduction studies explore a more distal segment of the nerve than do the studies on sural nerve conduction, where recording electrodes are placed at a more proximal site, i.e. the lateral malleolus.

Therefore, we are of the opinion that the median and ulnar nerve conduction studies may be more useful in the early detection of the impairment of the distal end of the nerve, mainly in the form of a decreased SNAP amplitude. Furthermore, they may also reveal focal entrapments, as the early, subclinical, sign of peripheral nerve damage, even when a generalized diabetic neuropathy is not yet evident [7].

Although we are aware that such an opinion about the particular usefulness of upper limb nerve conduction studies in DM is currently supported by limited evidence [3,4,7,8], we do feel that this is something that should be taken into account carefully when the nerve conduction criteria for diagnosis of diabetic neuropathies is being assessed”. As the aforementioned criterion of ≥1 abnormal attributes in ≥2 nerves has been reported to be the most useful to obtain a good sensitivity and specificity [2], we propose that the median and ulnar nerve, in their motor and sensitive component, be the two target nerves for an early diagnosis of diabetic neuropathies. Although our suggestions should be reappraised, in the light of further studies aimed at the comparison of upper and lower limb electrophysiological protocols for early diagnosis of diabetic neuropathies on larger samples of DM patients, we are of the opinion that the hands are of more interest than the foot for the neurophysiologist!

Conflict of interest

The authors declare no conflict of interest related to the present article.

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REFERENCES


