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Editorial

A New Window of Opportunity for Improved Diagnosis of Diabetic Polyneuropathy

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Introduction

Diagnosis of diabetic polyneuropathy (DPN), by far the commonest manifestation of diabetes mellitus (DM) in the nervous system, rests on careful clinical examination to reveal length-dependent, symmetrical, primarily sensory deficits in the distal parts of the lower extremities [1]. Clinical examination can be performed with minimal equipment by health care providers [1]. In the event of uncertainty or need for differential diagnosis and/or exclusion of other causes, the clinician should resort to quantitative confirmatory diagnostic modalities, such as nerve conduction studies [1]. However, improved diagnosis of DPN is necessary for two main reasons. First, we need simple tests to be used as screening tools to rule in/out DPN and to enable patient triage with appropriate referral of selected patients to specialised centres [2]. Secondly, we require tests sensitive enough to enable an early diagnosis of DPN and patient follow up after specific treatment or intensified glycaemic control. Thus, several new diagnostic tools have been developed [3]. Among these, it is especially the indicator test Neuropad [4] and in vivo corneal confocal microscopy (CCM) [5] that are useful, because each of them serves one of the two aforementioned purposes.

Neuropad is a simple indicator test, which is applied on the plantar aspect of the foot [4]. The principle of the test is measurement of skin humidity by a chemical reaction, which can be very easily visualised by a colour change. The colour of Neuropad is initially blue: if it changes to uniformly pink within 10 minutes, the test is normal [4]. In the opposite case, it is an abnormal result [4]. The test is so simple, that it can be reliably carried out by patients themselves or their families, enabling self-examination [6]. An abnormal Neuropad result has consistently been shown to exhibit a high sensitivity (65.1-100%) and a high negative predictive value (NPV) (63-100%) for the diagnosis of DPN [4]. In a recent meta-analysis including 3470 participants [7], positive and negative likelihood ratios were 2.44 and 0.22, respectively, confirming its excellent value mainly in excluding DPN. This diagnostic performance has been shown in newly diagnosed DM of both types [8], as well as in pre-diabetes [9]. There is also evidence that Neuropad can contribute to earlier diagnosis of DPN in type 2 DM [10]. Finally, it has been observed that the visual nature of the result can motivate patients to enquire about foot pathology and thus encourage patient education [4].

Conversely, CCM is an in vivo technique to quantify morphological alterations which is based on the visualisation of the small nerve fibres encountered in the cornea of the human eye [5, 11]. It is now known that the cornea harvests a multitude of such nerve fibres, which originate from the trigeminal nerve [5]. Using a laser scanning confocal microscope and trained personnel, one can measure corneal nerve fibre density (CNFD), corneal nerve fibre length (CNFL), corneal nerve branch density (CNBD), and other parameters of corneal nerve fibre morphology [5, 11]. In general, DPN is associated with corneal nerve fibre loss, which can be quantified as reduced CNFD and CNFL [5, 11]. Evidence of such corneal pathology as a marker of early neuropathic changes can be obtained in patients with recently diagnosed type 2 DM [11]. Interestingly, CCM is not invasive and can be easily repeated, enabling serial measurements to document improved innervation after optimisation of glycaemic control along with reduction of serum lipids and blood pressure [12]. Similar improvement has been documented following pancreas transplantation [13]. CNFD has been shown to

been shown to yield 82% sensitivity and 52% specificity for the diagnosis of clinically manifest DPN [14]. The diagnostic reliability of CCM can be enhanced by the use of modern software permitting image segmentation and automated measurement of nerve fibre parameters [5,11], but more experience is needed. Finally, CCM has begun to be appreciated as a test to detect neuropathy in diabetic children [15].

In conclusion, improved diagnosis of DPN is desirable, and several new tests have been developed for this purpose [3]. The Neuropad is an excellent screening tool mainly to exclude DPN by virtue of its relatively high NPV [4]. It may also be used for earlier diagnosis and patient self-examination [6]. CCM is a sophisticated modality which can be employed for early diagnosis and patient follow-up after treatment [5,12]. Both modalities represent a valuable new opportunity for improved diagnosis of DPN and merit more widespread clinical application.

Conflict of interest

NP and DZ have served as members in the scientific advisory board of Trigo Care International, distributor of Neuropad.

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