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Assessment of diabetic neuropathy using the NC-stat® DPNCheck™ device: *significant associations with the modified LDIflare method and clinical neuropathy scoring*

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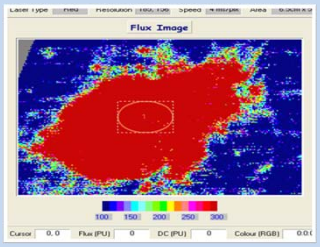
Introduction

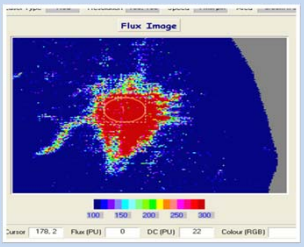
- Peripheral neuropathy is a common complication of diabetes. In addition to history and clinical examination, a variety of simple bedside methods can be used to detect neuropathy, of which, probably the Semmes Wenstein 10g-monofilament is probably the most commonly used. However, there is an unmet need for an objective and standardised test for diabetic peripheral neuropathy (DPN) that can also be used for monitoring for progression of DPN.
- The NC-stat® DPNCheck™ device (NeuroMetrix, Massachusetts) has been proposed to be a rapid, low-cost, point of care test for the assessment of diabetic peripheral neuropathy (DPN). It is a hand-held device which measures sural nerve conduction velocity (SNCV) and sensory nerve action potential (SNAP) amplitude.
- The laser Doppler imager (LDI) flare technique is a sensitive method of assessing small neural fibre function (SNF) and measures the axon-reflex-mediated neurogenic flare after heating. It has a good correlation with intra-epidermal nerve fibre density and is more sensitive than quantitative sensory testing.

NC-stat® DPNCheck™ device

The laser Doppler imager (LDI)



LDIflare in healthy volunteer



LDIflare in severe DPN

Aims

- This study evaluates the efficacy of the NC-stat® DPNCheck™ device in the assessment of DPN by comparing it with two established methods based on different pathophysiological basis:
  a. the modified LDIflare method as a marker of early SNF.
  b. Neuropathy Disability Scoring (NDS) which is a clinical neuropathy scoring based primarily on large fibre assessment.

Methods

- 135 patients with diabetes were recruited, 66 Type-1 Diabetes and 69 Type-2 Diabetes. Additionally, 65 healthy volunteers (HV) were also recruited.
- All participants underwent symptom evaluation and clinical examination for DPN. Based on the NDS, the DPN status was categorised into none (0-2), mild (3-5) moderate (6-8) and severe (9-10). Additionally, The NC-stat® DPNCheck™ was carried in the same foot where the modified LDIflare was performed.
- Using linear regression analysis (ANOVA), correlations between NC-stat® DPNCheck™ and the modified LDIflare and NDS categories were sought.

Results

- Average age (±SD) of the 136 patients was 47.93 (±14.03) years of which males were 75 (49.11±15.03 years) and females were 60 (46.45±12.63 years).
- The correlations outcomes between the NC-stat® DPNCheck™ device and modified LDIflare and NDS are shown in the table below:

Category	Mean age (yrs ± SD)	LDIflare (cm^2 ± SD)	NC-stat® DPNCheck™ vs. LDIflare		NC-stat® DPNCheck™ vs. NDS	
			SNCV (m/s)	SNAP (µv)	SNCV (m/s)	SNAP (µv)
No DPN *(n=51)*	39.31±12.82	7.62±1.62	49.84±8.67 *p=0.043*	17.31±9.93 *p=0.048*	*p=0.025*	*p=0.035*
Mild DPN *(n=30)*	48.03±9.89	5.95±1.43	40.85±8.31 *p=0.019*	11.37±4.89 *p=0.022*	*p=0.016*	*p=0.022*
Moderate DPN *(n=31)*	53.53±11.45	4.71±0.95	32.00±6.82 *p=0.001*	5.54±3.78 *p=0.004*	*p<0.0001*	*p=0.015*
Severe DPN *(n=15)*	62.40±11.99	2.74±1.05	23.60±8.99 *p<0.0001*	2.53±2.87 *p<0.0001*	*p<0.0001*	*p=0.008*
All DM patients *(n=135)*	47.93±14.03	5.87±2.10	39.77±12.26 *p=0.004*	10.95±8.88 *p=0.008*	*p<0.0001*	*p=0.004*
HV *(n=65)*	38.92±15.15	9.17±2.18	50.40+5.84 *p=0.005*	18.43+4.34 *p=0.013*	- *(no NDS outcomes)*	- *(no NDS outcomes*

- Significant correlations were observed between the NC-stat® DPNCheck™ device and NDS across all patients and within each sub-group. This further proves that the device correlates well with clinical findings related to large fibre function as has been shown previously *(Perkins et al)*.
- The NC-stat® DPNCheck™ device correlated significantly with the modified LDIflare method across all NDS groups but within each group the correlation becomes stronger with progression of neuropathy.
- It is of interest to note that similar SNCV's and SNAP's were observed between the no DPN (NDS≤2) and HV categories. However, the LDIflare size was significantly smaller (p<0.001) in the former group confirming our previous findings that in diabetes subjects without clinical DPN, SFN develops much earlier than large fibre neuropathy.

Conclusions

- Our results show that the NC-stat® DPNCheck™ device is a sensitive method of diagnosing early DPN and performs consistently as large fibre neuropathy progresses.
- It is not surprising to note that the relationship between the NC-stat® DPNCheck™ device and the modified LDIflare becomes stronger with progression of DPN since large fibre function can be normal in the presence of early small fibre dysfunction. The modified LDIflare is a sensitive test for small nerve fibre function while both the NC-stat® DPNCheck™ device and NDS predominantly reflect large fibre function.
- We conclude that the NC-stat® DPNCheck™ is an excellent adjunctive tool in assessment of DPN, especially in the busy clinical setting. It is a compact and ergonomic hand-held device, designed for ease-of-use and can aid in the early detection, confirmation, and monitoring of DPN.