Role of High-Resolution Ultrasonography of Ulnar Nerve in the Evaluation of Diabetic Peripheral Neuropathy

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ABSTRACT

BACKGROUND

Diabetic peripheral neuropathy is a long term complication of diabetes. Traditionally, clinical history, physical examination and electro physiological studies were relied upon for diagnosis. Currently, High resolution ultrasonography has come into picture in the diagnosis of peripheral neuropathy due to the ease, time saving ability and noninvasiveness of the procedure. We wanted to correlate the cross-sectional area and maximum thickness of nerve fascicles of the ulnar nerve with the presence and severity of diabetic peripheral neuropathy.

METHODS

A retrospective study was conducted between October 2018 and January 2019. The study group consisted of 85 type 2 diabetic patients. 55 Diabetic patients with clinical signs and symptoms of peripheral neuropathy were assigned to Group I. Group II comprised of 30 diabetic patients with no clinical signs and symptoms of peripheral neuropathy. 70 healthy volunteers were also recruited for the study, and assigned to Group III. The cross sectional area and maximum thickness of nerve fascicles of the ulnar nerve were measured at every predetermined site.

RESULTS

The cross sectional area of the ulnar nerve was measured at three sites (inlet of the cubital tunnel, outlet of the cubital tunnel and Guyon tunnel). The mean cross sectional area and maximum thickness of nerve fascicles of the ulnar nerves in the above three sites in Group I compared with both Group II and III was significantly larger, and statistically significant correlation was found with the Toronto Clinical Neuropathy Score ($p<0.001$). The Group II patients also had a significantly larger mean cross sectional area and maximum thickness of nerve fascicles than Group III.

CONCLUSIONS

High resolution ultrasonography of ulnar nerve is an easy non-invasive tool for the early diagnosis of diabetic peripheral neuropathy by assessing the cross sectional area and maximum thickness of nerve fascicles.

KEYWORDS

Ulnar Nerve, Peripheral Neuropathy, High Resolution Ultrasonography

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BACKGROUND

Type 2 diabetes mellitus (T2DM) has reached epidemic proportions in India. It is estimated that by the year 2030 there will be nearly 80 million Indians with T2DM in the country.[1] Diabetic polyneuropathy is a long-term and insidious complication of diabetes. The prevalence of diabetic peripheral neuropathy varies greatly in different studies ranging from 8% to 59%.[2,3,4] Poor control of blood glucose levels serves as a major risk factor in the development of diabetic polyneuropathy. Hyperglycaemia results in osmotic swelling of the nerves leading to axonal and myelin sheath damage, finally triggering the onset of neuropathy.[5] Traditionally, neuropathy was diagnosed based on clinical history, physical examination and electrophysiological studies. Several scoring systems have been developed to reflect the presence and severity of diabetic peripheral sensorimotor neuropathy, including the Toronto clinical neuropathy scoring system which encompasses the symptoms, sensory tests and reflex scores for the assessment.[6]

Recently, High Resolution Ultrasonography (HRU) has come into the foray in the evaluation of diabetic peripheral neuropathy. The peripheral nerves have a distinct honeycomb appearance in the transverse scan and on a longitudinal scan appear as multiple parallel hypoechoic bands separated by hyperechoic perineurium. In addition to the characteristic appearance they are superficial in location which makes them easily accessible for HRU. There is no patient discomfort, nor any radiation exposure and the nerves can be scanned for a long period of time.[7,8,9,10]

METHODS

After approval from the Institutional ethics review committee, a hospital based cross sectional study was conducted between October 2018 and January 2019. The study group consisted of 85 type 2 diabetic patients presenting to the Departments of Radiodiagnosis were recruited for the study, and provided their written informed consents. They were divided into two groups. Diabetic patients with clinical signs and symptoms of peripheral neuropathy were assigned to Group I, consisting of 55 patients. Group II comprised 30 diabetic patients with no clinical signs and symptoms of peripheral neuropathy. 70 healthy volunteers were also recruited for the study, and assigned to Group III. We excluded patients with previous ulnar nerve surgery, polyneuropathy, and acute traumatic aetiology. Ultrasonography was performed with performed with Philips Affiniti 50G using a linear array transducer (5-12 MHz).

The CSA of the ulnar nerve was measured by tracing along the hyperechoic rim of the nerve (Figure 1). The CSA of the ulnar nerve was measured at three sites (inlet of the cubital tunnel (ICT), outlet of the cubital tunnel (OCT), Guyon tunnel (GT)), and the difference in the CSA between the three groups was calculated and the maximum thickness of the nerve fascicle (MTNF) was calculated in the transverse view of the ulnar nerve by the largest antero-posterior dimension of the largest hypoechoic area (Figure 2). Each measurement was taken three times and the average was recorded.[11] A radiologist blinded to all participant information performed the ultrasound studies. The severity of the peripheral neuropathy was calculated using the Toronto Clinical Neuropathy Score (TCNS). Out of 19 points, severity was graded as follows- 0–5: absent; 6-1: mild-moderate; >12: severe.[12,13] Demographic information, including age, sex, weight and HbA_{1c} levels was recorded for all patients.

Statistical Analysis

The mean CSA and MTNF of the ulnar nerve in all three groups were compared using SPSS 20.0 software. Multiple mean comparison was analysed by one-way analysis of variance (ANOVA) followed by a post hoc LSD test. The correlations with HbA_{1c} levels and TCNS were identified using Pearson correlation coefficient.

RESULTS

Clinical and Demographic Characteristics	Group I (N=55)	Group II (N=30)	Group III (N=70)
Age in years (Mean ± SD) Range	60.1 ± 11.11 (40-89)	46.24 ± 6.43 (33-60)	39.64 ± 11.12 (24-72)
Duration of diabetes in years (Mean ± SD) Range	14.92 ± 7.12 (5-39)	7.82 ± 4.31 (1-19)	
Male-Female	34: 21	18: 12	42: 28
Weight in kg (mean ± SD) Range	79.92 ± 9.8 (54-97)	64.21 ± 9.89 (40-80)	65.45 ± 10.21 (41-85)

Table 1. Clinical and Demographic Characteristics of Patients

Group I – Diabetic Patients with Peripheral Neuropathy, Group II – Diabetic Patients without Peripheral Neuropathy, Group III – Nondiabetic Subjects

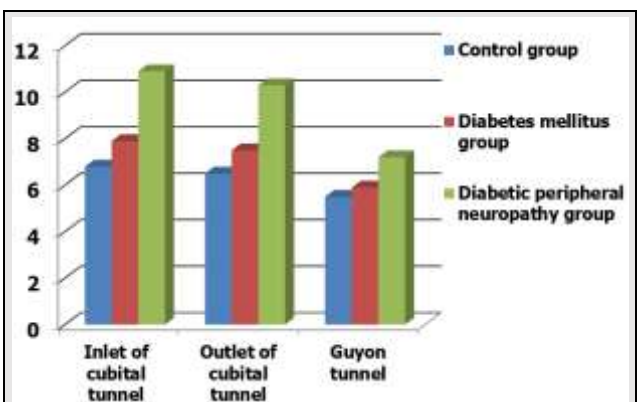

Table 2. The Cross Sectional Area of Ulnar Nerve in mm² of Three Groups Compared in Histogram

The study included 55 patients of diabetic mellitus presenting with symptoms of peripheral neuropathy (Group I), 30 patients of diabetes mellitus with no symptoms of peripheral neuropathy (Group II) and 70 healthy volunteers (Group III). The demographic and clinical characteristics of all the three groups are presented in Table 1. The mean CSA of the ulnar nerve was significantly larger ($p<0.001$) in Group I subjects than Groups II and III. The

mean CSA of the ulnar nerve was also larger (p<0.001) in Group II than in Group III (Table 2). The mean MTNF of the ulnar nerve was larger (p<0.001) in Group I in comparison with Groups II and III. The mean MTNF was higher (p <0.05) in Group II than Group III (Table 3).

Group I demonstrated higher HbA1c values in comparison to the other groups, with a good correlation with CSA (r = 0.785; p <0.001) and MTNF (r = 0.683; p <0.001). Group I had the highest mean TCNS, with a statistically significant correlation with CSA (r = 0.613; p <0.001) and MTNF (r = 0.723; p <0.001) of the ulnar nerve. (Table 4).

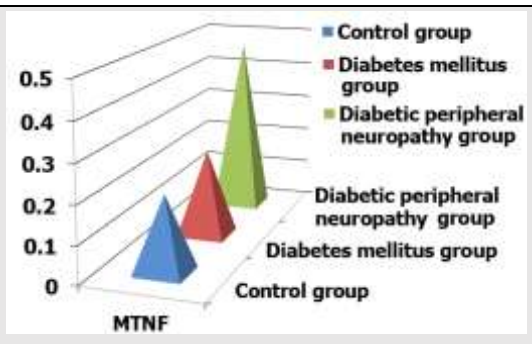

Table 3. The Maximum Thickness of Nerve Fascicles (MTNF) of Ulnar Nerve in mm of Three Groups Compared in Histogram

	Group I (N=55)	Group II (N=30)	Group III (N=70)
Mean CSA of ulnar nerve (mm2)	10.2 ± 2.66	7.6 ± 1.72	6.2 ± 1.1
MTNF (mm)	0.47 ± 0.09	0.23 ± 0.06	0.20 ± 0.05
Mean HbA1c levels (%)	7.84 ± 1.20	5.92 ± 0.69	
TCNS	10.14 ± 1.20	1.67 ± 0.69	

Table 4. Mean CSA, MTNF, Mean HbA1c Levels and TCNS Among the Three Groups

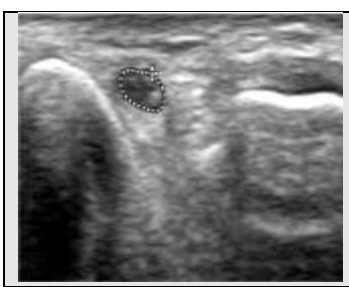

Figure 1. High resolution US of a 40-year old male nondiabetic. Inlet of the cubital tunnel. The nerve is the oval hypoechoic structure. The cross-section of the ulnar nerve is 6.3 mm²

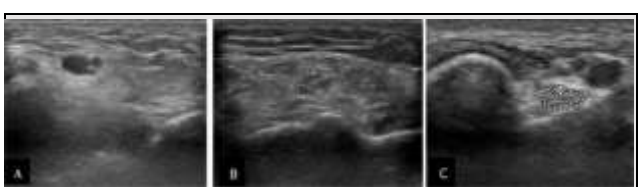

Figure 2- High resolution US of a 70-year old male diabetic patient with severe peripheral neuropathy (TCNS-15) A) Inlet of the cubital tunnel. The mean thickness of nerve fascicles (MTNF) of the ulnar nerve is 0.47 mm, the nerve is the circular hypoechoic structure. B) Outlet of the cubital tunnel. The nerve is the oval hypoechoic structure. The cross-section of the ulnar nerve is 10.2 mm². C) Guyon tunnel. The cross-section of the ulnar nerve is 7.2 mm²: the nerve is the oval hypoechoic structure.

DISCUSSION

Diabetes mellitus is one of the largest global non communicable disease due to the lifestyle changes. In India, the disease has reached epidemic proportions before the advent of imaging modalities, the diagnostic work-up of peripheral nerve disorders was based only on the evaluation of the clinical history, neurological examination and nerve conduction studies, F-waves and electromyography.[14] HRU and magnetic resonance imaging (MRI) are the frequently used imaging modalities for peripheral nerves. Due to its simplicity and ease of use, there is growing interest in the incorporation of HRU for the evaluation of peripheral nerves.[15] In HRU, healthy ulnar nerves appear as honeycomb like structures comprising of hypoechoic fascicles and hyperechoic surrounding epineurium. CSA is a more consistent index for measurement than the diameter as the nerve varies from a circular shape in the upper extremity to a flat oval shape at the wrist.[16,17]

In our study, the cross-sectional area of the ulnar nerve in the in three measuring sites (ICT, OCT, GT) was larger in Group I than in Group II and III. The enlarged nerves were hypoechoic or anechoic. Cubital and Guyon tunnel are partially fibrous and osseous tubular channels and the nerves are prone for compression in these osseous pipelines. However, an underlying mass lesion can also be a cause for nerve entrapment in diabetic patients and hence the possibility of one should not be excluded.[18,19] The ulnar nerve area increases in these points as diabetes affects the microcirculation and alters the host immunity.[20] The nerves demonstrate anatomical and functional changes in the preclinical stage itself, secondary to alterations in glucose metabolism.[21]

The mean CSA of the ulnar nerve in our study was significantly higher (P <0.001) at all three levels of examination in patients with DPN than the healthy volunteers i.e., 10.9 ± 2.87 mm^2 vs. 6.8 ± 1.49 mm^2 at inlet of cubital tunnel, 10.3 ± 2.95 mm^2 vs. 6.5 ± 1.31 mm^2 at the level of outlet of cubital tunnel, and 7.2 ± 2.27 mm^2 vs. 5.5 ± 1.43 mm^2 at the Guyon canal. The mean CSA of the ulnar nerve was also larger in Group II than in Group III, with p <0.001, with the mean CSA at three levels of examination in group II patients being 7.9 ± 2.95 mm2 at the inlet of cubital tunnel, 7.5 ± 2.95 mm^2 at the outlet of cubital tunnel and 5.9 ± 2.95 mm^2 at the Guyon canal. Findings were in concordance with another study by Watanabe et al who found that there is a significant increase in the CSA of the ulnar nerve in patients with DPN as compared with the controls.[22] Similar findings have been reported by Afsal M et al., Pitarokoili et al.,[23] who found that on HRU, there was a diffuse thickening of the peripheral nerve in these patients, and the mean CSA of the ulnar nerve was found to be significantly higher in patients with DPN than the normal matched controls.

One of the determinants of the hypoechoic area in CSA of peripheral nerves is the size of the nerve fascicles. The mean MTNF of the ulnar nerve was higher in Group I than Groups II and III, with p <0.001. MTNF in non-neuropathic diabetic patients was larger compared with control subjects (p<0.05), with statistically significant correlation between MTNF and the severity of neuropathy. Similar findings were observed by Ishibashi et al. where the morphological changes in the peripheral nerves of diabetic patients were

detected even before the onset of neuropathy, and were closely correlated with the severity of the disease.[24] As far as HbA_{1c} is concerned, it is an index of the average blood glucose level over the preceding weeks to months. Watanabe et al. studied the role of ultrasonography in diabetic peripheral neuropathy, concluding that there was no statistically significant correlation between HbA_{1c} levels and CSA of the peripheral nerves.[22] The likely reason may be the small sample size in their study. In our study, a significant correlation was observed between these two parameters, with $p < 0.001$ in Group I.

Compared with Groups II and III, Group I subjects showed the highest mean TCNS, with a good correlation with CSA ($r = 0.785$; $p < 0.001$) and MTNF ($r = 0.761$; $p < 0.001$) of the ulnar nerve. High-resolution ultrasonography has the potential to detect subclinical morphological changes in the nerves before the clinical presentation of neuropathy. Hence early initiation of the treatment can be considered.[25] Due to the ease of its availability HRU has the potential of becoming the modality of choice in evaluation of peripheral nerves and can supplement other diagnostic tools like nerve conduction studies. Further studies with larger number of patients are probably required. The study shows the utility of HRU in demonstrating changes of DPN which have been previously evaluated in a few studies.

CONCLUSIONS

HRU is a time saving and easy to use tool. Owing to their accessible superficial location and distinct sonological appearance, the nerves can be evaluated with ease in both healthy volunteers and diabetics. In our study we found that the diabetics without signs of neuropathy and diabetic peripheral neuropathy patients had a larger cross sectional area and mean thickness of nerve fascicles than healthy volunteers. HRU can detect morphological changes in the ulnar nerves even before the clinical onset of neuropathy.

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