THE CORRELATION BETWEEN PERIPHERAL NERVE CONDUCTION STUDY AND LEVEL OF URINARY ALBUMIN EXCRETION IN DIABETIC PATIENTS

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ABSTRACT

Objective: *The primary aim of this study was to evaluate the relation between neuropathy and diabetic nephropathy in patients.* ***Methods:*** *This is a cross-sectional study performed in 37 patients with diabetes. The UAE level is based on the albumin (µg)/creatinine (mg) ratio (ACR) measured in a random urine specimen. The NCSs were performed with standard electromyography (EMG) equipment provided by major manufacturer (Neuro-MEP-Micro of Neurosoft Company). Involved peripheral motor nerves are the median, ulnar, peroneal, and tibial nerve. Involved peripheral sensory nerves are the median, radial, ulnar, and superficial peroneal nerve.* ***Results:*** *After the study, we identified a significant negative correlation between level of UAE and action potential (AP), and between level of UAE and nerve conduction velocity (NCV) of motor nerves (R = - 0.33 to R = - 0.65, p < 0.05). We also found a significant negative correlation between level of UAE and NCV ((R = - 0.36 to R = - 0.48, p < 0.05), and a significant positive correlation between level of UAE and DSL (R = 0.37 to R = 0.74, p < 0.05) of sensory nerves.* ***Conclusion:*** *Our results suggested that the presence of microvascular diabetic complications are simultaneous, and the earliest presence is the DPN, especially abnormal NCS parameters.*

Keywords: *diabetic peripheral neuropathy (DPN), action potential (AP), nerve conduction velocity (NCV), diabetic kidney disease (DKD).*

1. INTRODUCTION

Diabetic kidney disease (DKD) is the most common cause of end-stage renal disease (ESRD), causing 45% of incident cases required renal replacement therapy in the United States [1], [3], [4], [5]. The incidence of diabetes worldwide is increasing, with an estimated prevalence of 380 million by 2025, hence the incidence of DKD is also increasing [2], [6], [8], [9], [5]. Several studies suggested that, there may be a relationship between appearance of DPN and impairment of kidney function [7], [10], [12], [13].

As known, DPN is a common complication of diabetes [14], [15]. However, prevalence estimates vary widely, most likely depending

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Received date: 2/5/2020
Reviewd date: 2/6/2020
Accepted date: 26/6/2020

on differences in patient selection, neuropathy definition, and methods of assessment. The routine evaluation of DPN is based on patient symptoms and a physical examination, which may include the Semmes-Weinstein monofilament and the 128-hertz tuning fork [11], [15]. However, nerve conduction studies (NCS) are the most sensitive and specific DPN detection method [6], [8], [10]. Their use is recommended for quantitative confirmation DPN in clinical practice. Expanded assessment to NCS has the potential for early diagnosis and improved outcomes.

The earliest presence of impairment of kidney function in diabetic patients is a urinary albumin excretion (UAE), microalbuminuria or macroalbuminuria [1], [2], and the major expression of DPN in NCS is a prolongation in distal latency and a reduction in nerve conduction velocity caused by axon damages [11], [14]. The primary aim of this study was to evaluate the relation between neuropathy and diabetic nephropathy in patients

2. METHODS

2.1. Subjects

Patients diagnosed with diabetes according to Standards of Medical Care 2019 (American Diabetes Association) [1].

- Fasting plasma glucose ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours.
- Or 2-h plasma glucose ≥200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.
- Or A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.
- Or In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

Total patients in this study were 37 outpatients with diabetes (17 men and 20 women; mean ± SD age 61.7 ± 11.4 years and duration of diabetes 7.5 ± 5.8 years)

2.2. Methods

- The cross-sectional study was performed in 37 outpatients at the Nephrology Department of HCMC University Medical Center.

- The UAE level is based on the albumin (µg)/creatinine (mg) ratio (ACR) measured in a random urine specimen. Microalbuminuria is defined as the ACR between 30 and 300 µg/mg; macroalbuminuriais defined as the ACR over 300 µg/mg [2].

- The NCSs were performed with standard electromyography (EMG) equipment provided by major manufacturer (Neuro-MEP-Micro of Neurosoft Company). Examinations were performed by trained electrophysiologists with extensive experience in recording and interpreting clinical data. Involved peripheral motor nerves are the median, ulnar, peroneal, and tibial nerve-parameters evaluated included the compound muscle action potential (AP) and motor nerve conduction velocity. Involved peripheral sensory nerves are the median, radial, ulnar, and superficial

peroneal nerve -parameters evaluated included the distal sensory latency (DSL) and sensory nerve conduction velocity [3].

The normal range of nerve conduction parameters are from Preston and Shapiro [16], is shown in the table 2.1:

Table 2.1. The normal values of nerve conductionMotor nerve

Motor nerve		Normal range
Median	AP	≥ 4 µV
	NCV	≥ 49 m/s
Ulnar	AP	≥ 7 µV
	NCV	≥ 49 m/s
Tibial	AP	≥ 4 µV
	NCV	≥ 41 m/s
Peroneal	AP	≥ 2 µV
	NCV	≥ 44 m/s

Sensory nerve		Normal range
Median	DSL	≥ 20 µV
	NCV	≥ 50 m/s
Ulnar	DSL	≥ 17 µV
	NCV	≥ 50 m/s
Radial	DSL	≥ 15 µV
	NCV	≥ 50 m/s
Superficial Peroneal	DSL	≥ 6 µV
	NCV	≥ 40 m/s

2.3. Data Analysis

Statistical analyses were performed with Stata software (version 10; Stata Corp, College Station, TX). To evaluate the correlation between peripheral NCS parameters and UAE level, we use Spearman rank correlation (R). Correlation coefficient values below 0.3 are considered to be weak; 0.3-0.7 are moderate; >0.7 are strong. A p-value less than 0.05 (typically ≤ 0.05) is statistically significant.

2.3. Ethical Research

All patient information is secure. All patients were taken part volunteer and agreement, not was obligatory. The patients were explained the content of the study, the benefits and the risks which they could to meet.

3. RESULTS AND DISCUSSION

Table 3.1 summarizes the data of the study participants. In this study, there were 23 patients with diabetic nephropathy (62.2%). Of which, 12 subjects are shown with microalbuminuria (32.5%) and 11 subjects are shown with macroalbuminuria (29.7%). Rate of patients with UAE in the group with duration of diabetes more than 5 years is higher than the group with duration of diabetes less than 5 years ($p < 0.05$). In addition, we identified a significant moderate positive correlation between duration of diabetes and level of UAE with correlation coefficient R = 0.35, $p < 0.05$. This result from our study was similar to result in the study of Diep Thi Thanh Binh et al. [5], in which rate of diabetes patients with microalbuminuria is 33.7% and the correlation between duration of diabetes and level of urinary protein excretion is $R^2 = 0.53$ (type 1), $R^2 = 0.04$ (type 2). In this study, we not differentiate type 1 or type 2 diabetes.

The correlation between peripheral NCS parameters and UAE level in diabetic patients are showed in Table 3.2a and Table 3.2b.

Table 3.1. The UAE opand duration of diabetes of participants.

UAE Level	Duration of diabetes			Total
	< 5 years	5 – 10 years	> 10 years	
Negative	9	3	2	14 (37.8%)
Microalbuminuria	5	2	5	12 (32.5%)
Macroalbuminuria	2	2	7	11 (29.7%)

Table 3.2a. The correlation between motor NCS parameters and UAE.

Nerve	Characteristic	Side	R	p
Median	AP	L	– 0.30	0.07
		R	– 0.36	< 0.05
	NCV	L	– 0.44	< 0.01
		R	– 0.40	< 0.05
Ulnar	AP	L	– 0.02	0.93
		R	– 0.08	0.65
	NCV	L	– 0.55	< 0.001
		R	– 0.53	< 0.001
Tibial	AP	L	– 0.36	< 0.05
		R	– 0.41	< 0.05
	NCV	L	– 0.65	< 0.001
		R	– 0.48	< 0.01
Peroneal	AP	L	– 0.33	< 0.05
		R	– 0.31	0.06
	NCV	L	– 0.59	< 0.001
		R	– 0.38	< 0.05

Our results identified a moderately up to strongly significant negative correlation (correlation coefficient R = -0.33 to R = - 0.65, $p < 0.05$) between level of UAE and AP,and between level of UAE and NCV of motor nerves. The strongest degree is belong to the correlation between level of UAE and NCV of tibial nerve (R = - 0.65, $p < 0.001$), and peroneal nerve (R = - 0.59, $p < 0.001$).

This result also found a moderately significant negative correlation (R = -0.36 to R = - 0.48, $p < 0.05$) between level of UAE and NCV of sensory nerves. The strongest degree is belong to the correlation between level of UAE and NCV of superficial peroneal nerve (R = - 0.48, $p < 0.01$). In addition, we identified a moderately up to strongly significant positive correlation (R = 0.37 to R =

0.74, $p < 0.05$) between level of UAE and DSL of sensory nerves. The strongest degree is belong to the correlation between level of UAE and DSL of radial nerve (R = 0.74, $p < 0.001$).

We divided peripheral nerve conduction characteristics in diabetic patients into three groups based on level of UAE: negative, microalbuminuria, and macroalbuminuria. Results are showed in Table 3.3a and Table 3.3b. Involved upper limb, we selected characteristics of median nerve and involved lower limb we selected characteristics of peroneal nerve. This results showed prolongation in distal latency, decrease in potential amplitude, and reduction in conduction velocity were significantly different. This result was similar to the result in study of Charles M et al. performed in 456 type 1 diabetic patients [4].

Table 3.2b. The correlation between sensory NCS parameters and UAE.

Nerve	Characteristic	Side	R	p
Median	DSL	L	– 0.16	0.35
		R	0.04	0.8
	NCV	L	– 0.08	0.64
		R	– 0.08	0.65
Ulnar	DSL	L	0.38	< 0.05
		R	0.56	< 0.001
	NCV	L	– 0.36	< 0.05
		R	– 0.46	< 0.01
Radial	DSL	L	0.74	< 0.0001
		R	0.65	< 0.0001
	NCV	L	– 0.46	< 0.01
		R	– 0.32	0.06
Superficial Peroneal	DSL	L	0.29	0.08
		R	0.41	< 0.05
	NCV	L	– 0.37	< 0.05
		R	– 0.48	< 0.01

Table 3.3a. The motor NCS parameters in three groups UAE

UAE Level	Median		Peroneal	
	AP*(mV)*	NCV *(m/s)*	AP *(mV))*	NCV *(m/s)*
Negative	10.59 ± 2.57	53.55 ± 6.38	3.39 ± 1.66	41.34 ± 2.66
Microalbuminuria	8.91 ± 2.70	51.67 ± 6.00	3.78 ± 1.43	37.91 ± 4.06
Macroalbuminuria	8.20 ± 1.85	47.29 ± 4.50	2.37 ± 1.70	34.96 ± 5.72

Table 3.3b. The sensory NCSop parameters in three groups UAE

UAE Level	Median		Superficial Peroneal	
	DSL *(ms)*	NCV *(m/s)*	DSL *(ms)*	NCV *(m/s)*
Negative	3.35 ± 1.01	44.20 ± 12.25	2.40 ± 0.72	55.77 ± 12.4
Microalbuminuria	3.08 ± 0.77	48.03 ± 9.95	2.95 ± 0.88	46.30 ± 11.51
Macroalbuminuria	3.46 ± 0.76	42.04 ± 8.29	3.12 ± 0.83	42.23 ± 11.33

In this cross-sectional study performed in 37 patients with diabetes, we identified a significant negative correlation between level of UAE and AP,NCV of motor nerves. We also found a significant negative correlation between level of UAE and NCV, and a significant positive correlation between level of UAE and DSL of sensory nerves.

4. CONCLUSION

In summary, from this cross-sectional study, we identified a significant negative correlation between level of UAE and action potential (AP), and between level of UAE and nerve conduction velocity (NCV) of motor nerves (R = - 0.33 to R = - 0.65, $p < 0.05$). We also found a significant negative correlation between level of UAE and NCV ((R = - 0.36 to R = - 0.48, $p < 0.05$), and a significant positive correlation between level of UAE and DSL (R = 0.37 to R = 0.74, $p < 0.05$) of sensory nerves. The results of this study suggested that the presence of microvascular diabetic complications are simultaneous, in which the earliest presence is the DPN, especially abnormal NCS parameters. The presence of DPN may be a recommendation for the endocrinologist and nephrologist in early detection and treatment of DKD. Thus, peripheral NCS should be a routinely screened for microvascular complications in diabetic patients.

Acknowledgement

Support for this study was provided by research grants from the University of Medicine and Pharmacy at Ho Chi Minh City.

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TÓM TẮT

SỰ TƯƠNG QUAN GIỮA DẪN TRUYỀN THẦN KINH NGOẠI BIÊN VỚI MỨC ĐỘ TIỂU ĐẠM TRÊN BỆNH NHÂN ĐÁI THÁO ĐƯỜNG

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Mục tiêu: *Mục đích chính của nghiên cứu là đánh giá mối liên quan giữa bệnh lý thần kinh và bệnh lý thận do đái tháo đường.* ***Phương pháp:*** *Nghiên cứu cắt ngang được thực hiện trên 37 bệnh nhân mắc bệnh đái tháo đường. Mức độ tiểu đạm được đo lường theo tỷ lệ ACR (albumin/ creatinine) trong mẫu nước tiểu ngẫu nhiên. Các chỉ số dẫn truyền thần kinh được thu thập từ máy đo điện cơ (EMG) Neuro-MEP-Micro. Các dây thần kinh vận động ngoại biên được khảo sát bao gồm dây giữa, quay, chày và mác sâu. Các dây thần kinh cảm giác ngoại biên được khảo sát bao gồm dây giữa, trụ, quay và mác nông.* ***Kết quả:*** *Chúng tôi đã xác định được mối tương quan nghịch có ý nghĩa giữa mức độ tiểu đạm với biên độ điện thế động (AP) và giữa mức độ tiểu đạm với tốc độ dẫn truyền (NCV) của các dây thần kinh vận động (R = - 0,33 đến R = - 0,65, p <0,05). Chúng tôi cũng tìm thấy mối tương quan nghịch có ý nghĩa giữa mức độ tiểu đạm với tốc độ dẫn truyền cảm giác (R = - 0,36 đến R = - 0,48, p <0,05) và mối tương quan thuận có ý nghĩa giữa mức độ tiểu đạm với thời gian tiềm cảm giác ngoại vi (DSL) (R = 0,37 đến R = 0,74, p <0,05).* ***Kết luận:*** *Kết quả của chúng tôi cho thấy sự xuất hiện của các biến chứng mạch máu nhỏ gần như là đồng thời, trong đó sớm nhất là bệnh lý thần kinh ngoại biên với sự bất thường của các chỉ số dẫn truyền cảm giác.*

Từ khóa: *bệnh lý thần kinh ngoại biên do đái tháo đường (DPN), điện thế động (AP), vận tốc dẫn truyền thần kinh (NCV), bệnh lý thận do đái tháo đường (DKD)*