Nerve conduction studies in patients with type 2 diabetes mellitus in Basrah

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ABSTRACT

Background: Diabetes mellitus has an effect on the peripheral nerves. Such effect may start as asymptomatic peripheral neuropathy.

Objectives: To assess the role of electrodiagnostic study in the diagnosis of patients with different types of diabetic peripheral neuropathy (DPN) and evaluate the usefulness of it in early detecting diabetic peripheral neuropathy in asymptomatic patients and to correlate the findings of nerve conduction study in patients with asymptomatic diabetic peripheral neuropathy with various risk factors.

Subjects and Methods: subjects were allocated into three groups: 50 normal (non-diabetics apparently healthy subjects without peripheral neuropathy), 50 asymptomatic DPN patients and 50 symptomatic DPN patients. Clinical questionnaire, blood sugar, neurological examination and nerve conduction studies were performed for each subject.

Results: This study showed that the prevalence of positive nerve conduction studies was 58% in asymptomatic diabetic patients, 100% for symptomatic diabetic patients and negative for control. The positive nerve conduction study findings in asymptomatic diabetic patients involved sensory more than motor fibers and the lower limbs nerves were affected more than that of the upper limbs. The most commonly involved nerve is the sural nerve sensory fiber which was more prevalent in old age patients (87.5%), patients with longer duration of diabetes (81.8%), over weight (71.4%), patient taking only oral antihyperglycemic drugs (76.9%) and in diabetic patients with poor glycemic control (84.2%) (86.3%) in fasting blood glucose (FBG) and HbA1c respectively. Using the logistic regression, only oral antihyperglycemic drugs (without insulin) and poor control HbA1c were significant predictors of abnormal nerve conduction.

Conclusion: Even in asymptomatic patients, nerve conduction studies show diffuse changes, in a predictable pattern. Electrophysiological finding correlate with age, duration of disease, glycosylated hemoglobin levels, fasting blood glucose, type of the treatment if only oral antidiabetic and body mass index.

Keywords: diabetes, asymptomatic, peripheral, neuropathy.

دراسة تخطيط الأعصاب لمرضى داء السكري نوع ٢

خلفية الدراسة: مرض داء السكري له تأثير على الأعصاب المحيطة وقسم منها يبدأ بدون أعراض اعتلال الأعصاب المحيطة.

الهدف من الدراسة: تقييم دور وجدوى تخطيط الأعصاب في مختلف أنواع اعتلال الأعصاب المحيطة السكري الكشف المبكر عن اعتلال الأعصاب المحيطية السكري في المريض بدون أعراض سريريه و ارتباط نتائج تخطيط الأعصاب لمرضى السكري بدون أعراض سريريه مع عوامل المؤثرة الأخرى.

الطريقة والمواد: العينات صنفت بثلاث مجاميع على الشكل التالي: ٥٠ شخص من الأصحاء ليس لديهم داء سكري و لا أعراض اعتلال الأعصاب المحيطة، و٥٠ شخص لديهم داء السكري نوع ٢ وليس لديهم علامات اعتلال الأعصاب المحيطة و٥٠ شخص لديهم

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مرض داء السكري و علامات اعتلال الأعصاب المحيطة. وقد خضعوا جميعهم إلى الاستبيان السريري وفحص السكر بالدم وفحص الأعصاب السريري و أجرى عليهم الاستقصاءات الكهروفسيولوجية لتخطيط الأعصاب المحيطة الكهربائي.

النتائج: وبينت هذه الدراسة أن معدل انتشار الاستقصاءات الكهروفسيولوجية لتخطيط الأعصاب المحيطة الكهربائي إيجابية ٥٨%للمرضى السكري الذين ليس لديهم أعراض اعتلال الأعصاب المحيطة و كانت ١٠٠% للذين لديهم إعراض و كانت نتيجة سلبية للأصحاء، وكان هذا الاعتلال العصبي المحيطي السكري لفئة مرضى السكري من غير أعراض وعند تقييم الأعصاب الحسية يظهر تدهورا ملحوظا في كفاءتها أكثر من الأعصاب الحركية و أعصاب الأطراف السفلى أكثر من الأطراف العليا ويعد العصب الربلي الحسي أكثر الأعصاب تأثيرا وتكون أكثر شيوعاً في مرضى كبار السن(٨٧,٥%) والمرضى المصابين بفترة زمنية طويلة (٨١,٨%)، ومرضى الوزن الزائد (٧١,٤%) والمرضي الذين يأخذون علاج الأقراص فقط(٧٦,٩%) عدم انتظام السكر في الدم لـ FBS (٨٤,٢%) و لـ HbA1c (٨٦,٣%). ومن خلال الطرق الإحصائية وجد ان عدم انتظام HbA1c والمرضى الذين يأخذون علاج الاقراص فقط بدون ابر الانسولين اكثر حلات تنبئا بوجود نتائج ايجابية في تخطيط الاعصاب.

الاستنتاج: قسم من المرضى من غير أعراض سريرية لعتلال الأعصاب المحيطة السكري يكون لديهم نتائج ايجابية عند أجراء تخطيط الأعصاب لهم وهذه النتائج ترتبط طرديا مع زيادة في العمر و طول فترة الإصابة بالمرض وعدم انتظام السكر بالدم و نوع العلاج إذا كانوا يأخذون أقراص فقط و زيادة مؤشر كتلة الجسم.

الكلمات المفتاحية: السكري، عديم الاعراض، محيطي، ضعف الاعصاب

INTRODUCTION

Diabetic peripheral neuropathy (DPN) is a descriptive term meaning a demonstrable disorder, either clinically evident or subclinical, that occurs in diabetes mellitus without other causes of peripheral neuropathy. About 60 to 70% of people with diabetes have some form of neuropathy.[1,2] Impairment of sensory motor axons and myelin sheath at the distal nerve ending already exists in early stages of diabetic peripheral neuropathy. Before symptoms arise electrophysiological test reveals impairment of peripheral nerves.[3] If the neuropathy is sensory, symptom as tingling, numbness, loss pain and loss temperature sensation are the main manifestations, while if the neuropathy is motor, then symptom as muscle weakness, wasting and paralysis are evident. [4] The mechanism of the DPN depend on how long exposure to high blood glucose, the mechanism either due to increase polyol flux leading to neuron cell lysis [5] or due to advanced glycation end products (AGE) of vessel wall that activate inflammatory

cascades, resulting in neural ischemia and cell damage and death.[6,7] also may be due to decreased effectiveness of the Vascular Endothelial Growth Factor.[8]

Electro diagnostic test (EDX):

Electrophysiological study of the peripheral nervous system is highly sensitive for defining the pattern and degree of nerve involvement and chronicity of a neuropathy. It is considered an extension of the neurological examination supplementing the clinical examination by providing additional precision, details, objectivity and delineate a variety of pathological changes that are clinically either obscure or undetectable. The Electromyography evaluation includes nerve conduction studies (sensory and motor) and the needle electromyographic examination of muscle.[5] The important electrodiagnostic test for early diagnosis of DPN by localization of lesion, distribution lesion, type of pathology, state the severity of the disease process and assessment

of prognosis and the effect of treatments. The present study was designed to assess the role of electrodiagnostic study in the diagnosis of patients with different types of diabetic peripheral neuropathy and to evaluate the usefulness of it in early detecting diabetic peripheral neuropathy in asymptomatic patients and to correlate the findings of nerve conduction study in patients with asymptomatic diabetic peripheral neuropathy with various risk factors.

SUBJECT AND METHODS

This cross sectional study was conducted at the College of Medicine, University of Basrah during the academic year 2016/2017 and was approved by the College Ethical Committee. Three groups of human subjects were included in this study collects from Al-Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) in AL-Faiha hospital and neuromedicine outpatient department in AL-Basrah General hospital. Electromyographic tests were carried on the three groups, the controls, asymptomatic DPN patients and symptomatic DPN patients. All of them were informed regarding the technique of the test and the aim of the study, and their consent was taken. Nerve conduction studies were performed on both upper and lower limbs. A detailed questionnaire was filled for each subject which included personal characteristics, family history, duration of disease, type of treatment, anthropometric measures, physical examination, biochemical measurements including fasting plasma glucose, post prandial plasma glucose and HbA1c, excluded anypatients had another type of peripheral neuropathy rather than diabetic peripheral neuropathy.

Electro diagnostic evaluation: Electro diagnostic examination included two components: Nerve Conduction Studies (NCS) and the needle electromyographic (EMG) study, were done at room temperature 25°C with MICROMED, KP 3.0 ® model 2003 using surface electrodes and needle electrodes performed by single investigator. It was done using conventional method with limbs kept warm, in (DM) patients and the control group were also measured. [9]

Nerve Conduction Studies: The distal sensory latency (DSL), sensory conduction velocity (SCV) and sensory amplitude (Amp) were measured for median, ulnar and sural nerves as well as distal motor latency (DML), motor conduction velocity (MCV), motor amplitude (Amp) were measured for median, ulnar and common peronal nerve. F-wave for right common peronal nerve and right ulnar nerve, H-reflex for right and left posterior tibial nerves.

Needle-Electromyography: The electrical motor unit recorded by the EMG needle is called the motor unit action potential (MUAP) and represents only a portion of the anatomic motor unit. It was done only for asymptomatic & symptomatic diabetic patient only, & choice 3 muscles: right first dorsal interosseous as upper limb muscles. left extensor digitorum brevis and right tibialis anterior as lower limb muscles.

Staged severity of various types of DPN according to electrodiagnostic studies:[10]
1. Early stage of neuropathy if H-reflex is low or not present.
2. Mild axonal sensory neuropathy if sensory nerve action potential amplitude (SNAP) is reduced.
3. Mild axonal sensorimotor neuropathy if sensory nerve action potential and compound muscle action potential (CMAP) were reduced.
4. Moderate axonal sensorimotor neuropathy if associated with delay latencies in addition to sensory nerve action potential and compound muscle action potential were reduced.
5. When the amplitude of the motor response are significantly involved with needle EMG changes of axonal degeneration or we don't obtained motor response we considered as advanced.
6. demyelinating neuropathy when nerve conduction velocity Decline more than 70% of the normal value.

RESULTS

Characteristics of the study population

There are no statistically significant differences between the various characteristics of subjects recruited for the 3 groups; control group, asymptomatic and symptomatic diabetic groups in terms of age, gender, height, weight, body mass index and family history education level while significant in term of HbA1c, fasting blood glucose, type of treatment, duration and Associated diseases (Tables-1).

Table 1. Characteristics of the study population.

Parameters	People with no diabetes n =50	Patients with no symptoms of PNP* n =50	Patients with symptoms of PNP* n =50	P Value
Age in years mean ± SD	52 ± 7.6	54.6 ± 9.2	55.12 ± 9.5	0.328
Gender = n(%)				0.898
Males	34 (68%)	30 (60%)	28 (56%)	
Females	16 (32%)	20 (40%)	22 (44%)	
Education = n(%)				0.06
Illiterate	9 (18%)	10 (20%)	15 (30%)	
Primary school**	15 (30%)	18 (28%)	19 (38%)	
Secondary school	14 (28%)	14 (36%)	11 (22%)	
Basic university & Higher education	12 (24%)	8 (16%)	5 (10%)	
Height in cm mean ± SD	169.89 ± 6.6	168.8 ± 6.3	168.1 ± 7.4	0.638
Weight in Kg mean ± SD	67.93 ± 8.6	68.98 ± 16.3	68.12 ± 15.21	0.906
Body mass index in Kg/m^2 mean ± SD	23.46 ± 2.1	24 ± 4.8	23.92 ± 4.2	0.765
Associated diseases = n(%)				
NO associated disease		27 (54%)	17 (34%)	< 0.001
Hypertension		14 (28%)	17 (34%)	
Ischemic heart disease		3 (6%)	4 (8%)	
Sickle cell anemia		4 (8%)	7 (14%)	
HT and IHD		1 (2%)	3 (6%)	
HT and SCA		1 (2%)	2 (4%)	
Type of treatments = n(%)				
Oral antihyperglycemic		43 (86%)	38 (76%)	< 0.001
Oral + Insulin		7 (14%)	12 (24%)	
Fasting blood glucose in mg/dl	93.65 ± 9 (80-116)	151.9±16 (130-184)	167.22 ± 38.7 (133-320)	
Controlled=n(%)	50 (100)	0	0	< 0.001
Accepted=n(%)	0	31 (62)	27 (54)	
Poor=(%)	0	19 (38)	23 (46)	
HbA1c % mean ± SD	5.48 ± 0.29% (4.7-6.3)	8.2 ± 1.4% (6.1-11)	9.4 ± 1.67% (6.8-12.7)	
Controlled=n(%)	50 (100%)	4 (8%)	0	< 0.001
Accepted=n(%)	0	24 (48%)	27 (54%)	
Poor=(%)	0	22 (44%)	23 (46%)	
Duration of D.M. in years mean ± SD		6.3 3.2	7.86 ± 4.08	< 0.001

* PNP: Peripheral neuropathy,

** Including those who just read and write

Finding of the Nerve conduction studies
in all groups:

The electro-diagnostic studies were positive in all patients in the symptomatic group and 29(58%) of the asymptomatic group while negative for all control group individuals, (Table-2).

Table 2. Prevalence of positive & negative nerve conduction study for all groups.

Nerve conduction studies findings	Control (%)	Asymptomatic DPN* (%)	Symptomatic DPN* (%)
Positive	0(0%)	29(58%)	50(100%)
Negative	50(100%)	21(42)	0(0%)
Total	50	50	50

***DPN: diabetic peripheral neuropathy**

Factors predicting nerve conduction abnormalities

In order to identify the independent predictors of nerve conduction abnormality among asymptomatic patients, we used logistic regression analysis as shown in (Table-3). The dependent variable was the state of nerve conduction (Abnormal versus normal). The independent variables entered in the equation are shown in (Table-3). Only two variable could predict nerve conduction abnormality these are type of treatment and HbA1c.

Table 3. Logistic regression analysis to predict nerve conduction study among asymptomatic patient.

Independent variables	B	P value	Or (exp)	Confidence limit	
				Lower	Upper
Significant predictors					
Type of treatment (Mixed)	2.110	0.008	8.249	1.715	39.679
HbA1c	1.123	0.031	0.325	0.118	0.901
Age	0.008	0.913	0.992	0.857	1.148
Gender	1.279	0.213	3.594	0.48	26.925
BMI	0.097	0.29	0.907	0.757	1.086
Duration	0.231	0.252	0.794	0.535	1.178
FBS	0.38	0.316	1.039	0.964	1.12

Abnormal electrodiagnostic findings in asymptomatic and symptomatic DPN

Distribution of diabetic peripheral neuropathy with abnormal nerve conduction finding in 29 asymptomatic DPN and 50 symptomatic DPN (Table-4).

Table 4. Distribution abnormal nerve conduction studies according to nerves.

Abnormal nerve parameters	Asymptomatic dpn	Symptomatic dpn
H reflex	5 (17.2%)	3(6%)
H reflex-sural	10(34.4%)	15(30%)
H reflex sural-peroneal	4(13.8%)	7(14%)
H reflex Sural Peroneal median(M*&S) ulnar (M&S)**	4(13.8%)	9(18%)
H reflex- Sural Peroneal- median (M&S)- ulnar (S)	1(3.4%)	——————
H reflex- median (M&S)	5(17.2%)	——————
H reflex peroneal median (S) ulnar(S)	——————	8(16%)
H reflex peroneal ulnar (M&S)	——————	1(2%)
H reflex median (M&S) ulnar (M&S)	——————	7(14%)

DPN: diabetic peripheral neuropathy, *M: motor, **S: sensory
H reflex (right and left tibial nerve) is prolong or absent in all positive nerve conduction studies.

Incidence and severity of the abnormal electro diagnostic findings

Regarding asymptomatic diabetic peripheral neuropathy including early stage of neuropathy in 5(17.2%) patients, mild sensory axonal neuropathy in 10(34.5%) patients, mild sensori-motor axonal neuropathy in 8(27.5%) patients, moderate sensorimotor axonal neuropathy in 6(20.6%) patients while in symptomatic diabetic peripheral neuropathy including early stage in 3(3%) patients, mild sensory axonal neuropathy in 15(30%) patients, mild sensorimotor axonal neuropathy in 11(22%) patients, moderate sensorimotor axonal neuropathy in 19(38%) patients and advance sensory motor axonal neuropathy in 2(4%) patients (Table-5)

Table 5. Incidence and severity of the abnormal electrodiagnostic findings.

Severity	Asymptomatic* DPN (N=29) (%)	Symptomatic* DPN (N=50)(%)
Early	5(17.2%)	3(6%)
Mild sensory axonal neuropathy	10(34.5%)	15(30%)
Mild sensorimotor axonal neuropathy	8(27.5%)	11(22%)
Moderate sensorimotor axonal neuropathy	6(20.6%)	19(38%)
Advance	0(0%)	2(4%)

*Data are presented as the number of patients with abnormal electrodiagnostic findings (%).

DISCUSSION

DPN is a common microvascular complication of diabetes mellitus that eventually affects the majority of diabetic patients. Symptoms may develop at any degree of neuropathic impairment or may not. Nerve conduction studies had been proved to be the more powerful indicator for neuropathy than clinical examination especially in the asymptomatic groups.[11] Its worldwide prevalence seems significant and is associated with significant morbidity and disability. [12] In our study the prevalence of neuropathy in asymptomatic diabetic peripheral neuropathy according to NCS finding was 58%, while in Kjersti, et al study in Bangladesh they reported an overall prevalence of DPN of 19.7% ,[13] Uwakwe et al study in Nigeria found a prevalence rate of DPN is75%.[14] In Rochester DPN study neuropathy presented in 66% of diabetic patients.[15] While in Khaled et al in Egypt the prevalence of DPN among studied subjects was 29.7%.[16] The differences in prevalence of DPN among different countries may be attributed to methodological differences in diagnosing DPN, ethnic differences in the prevalence of DPN attributed to different exposure to risk factors of DPN and different patients. In our study only two variables could predict nerve conduction abnormality, these are HbA1c level and type of treatment. Significant association between poor glycemic control and the development of DPN

in aymptomatic group had been found and 86.3% of asymptomatic patients had been found to have high Hb A1c level. This agrees with Arindam study [17] where prolonged and poorly controlled DM was the most significant factors associated with DPN. Also Kaur study in India had found that maintenance of aggressive control of HbA1c is the key to prevent and delay the DPN.[18] The association between poor glycemic control and the development of DPN can be explained by the well-known harmful metabolic, inflammatory and oxidative effects of hyperglycemia on the nerves fiber beside the damages to small blood vessels (micoangiopathy) which lead to nerve fibers damage.[19] Also in our study, significant association between type of treatment and the development of DPN in asymptomatic group had been found and 76.9% of asymptomatic patients who take only oral antidhyperglycemic drugs had been found to have DPN in compare to 37.5% of asymptomatic patients who take mixed treatment with Insulin & oral antidhyperglycemic drugs which is consistent other studies.[20] In our study the most common changes on nerve conduction study in both asymptomatic and symptomatic diabetic peripheral neuropathy groups were abnormality of H- reflex and sural nerve. Regarding the severity of nerve conduction studies, mild sensory axonal neuropathy were the most

common in asymptomatic diabetic peripheral neuropathy group followed by mild sensori motor axonal neuropathy while in symptomatic diabetic peripheral neuropathy group moderate sensori- motor axonal neuropathy were the most common followed by mild sensorimotor axonal neuropathy, this may indicate that peripheral neuropathy start early with sensory changes then with the chronicity of the disease, motor nerves involve. In both groups the nerve conduction studies abnormalities in lower limbs were more common than upper limbs, the F-wave was intact for all patients while the H-reflex was unobtainable or prolonged in all patients with peripheral neuropathy. These findings are consistent with study by Rainha J. de souza et al[21] and Misra et al[22] which show similar findings in their study. This can be explained by the fact that diabetic peripheral neuropathy is a type of metabolic neuropathy and the pattern of this neuropathy is usually length depended peripheral neuropathy and it is usually start in the lower limb and then ascend up to involve the upper limbs and also it is usually involve first the sensory nerves and then involve the motor nerves which is in agreement with the findings obtained by our study.

In conclusions, the risk of developing peripheral neuropathy in asymptomatic diabetic patients is fairly high and significantly related to glycemic control. Absence of symptoms didn't exclude DPN and a significant proportions of those patients were in danger of developing foot ulcers.

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