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FACTORS THAT INFLUENCE NERVE CONDUCTION IN DIABETIC PATIENTS

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Abstract

The alteration in nerve conduction is considered one of the important complaints of patients who are suffering from diabetes mellitus nowadays. Therefore, we conduct this study which aimed to evaluate the nerve conduction velocity and amplitude in diabetic patients and assess the effects of the patients' age, severity and duration of diabetes on nerve conduction impairment. A case control study, the studied sample were 200 persons, 150 diabetic patients (93 males and 57 females) and the control group consisted of 50 participants (32 males and 38 females). All the patients attended the neurophysiology outpatient department of Al-Sader Teaching Hospital in Basrah city. The diabetic participants were selected at random from age, diabetes duration, and sex. Regarding the ages and exclusion criteria of the controls were ranged same as the diabetic. All participants were interviewed and a questionnaire form was filled prior to examination. Both the diabetic patients and the controls were subjected to the same electrophysiological and laboratory investigations.

The results of the study showed a significant decrease in nerve conduction velocity and amplitude in diabetic patients comparing to controls in all the examined nerves. Furthermore, there was a significant association between advancing age and longer-duration of diabetes with the reduction of conduction velocity and amplitude. Also, a significant inverse correlation between increased severity of diabetes disease (HbA1c level) and decreasing of both conduction velocity and amplitude. However, the study demonstrated no statistical significant difference between patients and controls regarding the gender. In conclusion, the age of the patients, duration of the disease and the severity of diabetes (hyperglycemia control) are playing a crucial role as risk factors in developing of peripheral neuropathy in diabetic patients.

Introduction

Diabetes mellitus is a chronic disease, which develops when pancreas is not producing enough insulin, or when the body cannot effectively use the insulin it produces[1]. Diabetes mellitus complications consist of both micro-vascular (neuropathy, nephropathy, and retinopathy) and macro-vascular (atherosclerotic) disease[2]. The most common micro-vascular complication of diabetes is known as peripheral neuropathy[3]. The risk of building a diabetic neuropathy is related to both the duration and magnitude of hyperglycemia[4]. Till now the nerve conduction studies(NCS) exist as the most dependable, sensitive and accurate measurement of peripheral nerve working in diabetic neuropathy[5]. Diabetic peripheral neuropathy is connected with changes in both nerve conduction velocity and amplitude[6]. Even though the conduction velocity variation may be an earlier hint of peripheral neuropathy, reduced amplitude is the most clinically reliable, due to its direct indicative of myelinated nerve fibre damage[7].

Patients and Methods

A total of 220 persons were divided into 2 groups, the diabetic patients group which consisted of (150) diabetic patients

(93 males and 57 females), the patient's age ranged from 20 to>60 years old and with a duration of diabetes ranged from (≤ 5 to >15) years.

These participants were selected at random from age, diabetes duration, and sex. All the patients attended the electro neurophysiological outpatient department of Al-Sader Teaching Hospital in Basrah city.

The controls group consisted of 70 participants, consist of (38 females and 32 males). Regarding the age of the control was ranged same as the diabetic 20 to >60 years old. These controls were from the medical staff of the hospital and from volunters. Exclusion criteria which selected to the controls group were similar to the exclusion criteria that were selected to the diabetic group. The controls group were subjected to the same testing and investigations as the diabetic group simultaneously

All participants were interviewed and a questionnaire form was full filled prior to examination. The questionnaire form includes the following: The patient general information: including (sex, age, marital status, occupation, address, educational status), duration of diabetes mellitus, types of treatment and any other associated diseases .

Nerve conduction studies (NCS) were performed in neuro-physiological department in Al-Sader Teaching Hospital by trained electrophysiologists with extensive experience in recording and interpreting clinical data. All the patients were examined in a comfortable supine position with their upper and lower limbs flexed 10-15 o at the elbow and the knee joints respectively. Micromed System-plus EMG machine was used for electrophysiological analysis of nerve fibers conduction studies. This system includes eight channels preamplifiers and built-in two isolated stimulators with separate jacks. The stimulus intensity can be manually adjusted (0-99 mA), and the evoked responses can be displayed on the monitor, on which four channels can be displayed at the same time. The machine also contains an audio-amplifier which helps to localize the site of stimulation of the nerve in case of the NCS.

For all examined nerves in this study (common peronieal, tibial, sural, median and ulnar nerve), surface electrodes were used for the stimulation as well as for the measuring and recording of nerve conduction velocity and amplitude.

The Statistical Package for the Social Sciences (SPSS) was used, the arithmetic mean and standard deviation of distribution of each of the parameters were calculated. The independent sample T-test program was used to get the significance level (P-value) for all of the parameters tested. A ($P<0.05$) is considered significant, ($P<0.001$) is highly significant and ($P>0.05$) is non-significant.

Results

The total number of the patients was 150 patients, 93 (62%) males and 57(38%) females, the majority were males. The age of these patients ranged from 20 to >60 years, for comparison purposes, the studied patients were divided into 5 age groups: 20-30 years, 31-40 years, 41 -50 years, 51-60 years and >60 years. The majority of the patients aged between 51-60 years old, has a number of 50 patients which represents approximately (33.3%) of total patients groups. The duration of illness ranged from ≤5 to >15 years, it has been divided into 4 categories as the following : ≤5 years, 6-10 years, 11-15 years, >15 years. The highest number was 46 patients which represents approximately (30.67%) of the total patients groups at duration >15 years, as clarified in table I.

Table I: Characteristics of the patients included in this study

Characteristic of patients		Number	(%)
Sex	Male	93	62
	Female	57	38
Age group	20-30	13	8.67
	31-40	20	13.33
	41-50	41	27.33
	51-60	50	33.33
	>60	26	17.33
Duration	≤ 5	20	13.33
	6-10	43	28.67
	11-15	41	27.33
	>15	46	30.67

The controls total number was 70 persons, the majority of them were females 38 (45.29 %) while males were 32(45.71 %). The general features of controls were summarized in table II.

Table II: Characteristics of the controls included in this study

Characters of controls		Number	(%)
Sex	Male	32	45.71
	Female	38	45.29
Age group	20-30	9	12.86
	31-40	15	21.43
	41-50	12	17.14
	51-60	18	25.71
	>60	16	22.86

The electrophysiological studies of the studied sample showed a significant decrease in nerve conduction velocity and amplitude in diabetic patients comparing to controls in all the examined nerves (common peroneal, posterior tibial, sural, median and ulnar). As shown in table III.

Table III: Comparison all examined nerves conduction parameters for patients and controls.

Nerve	Patients nerve velocity (m/sec) Mean ± SD	Patients amplitude (mv.) Mean ± SD	Controls nerve velocity (m/sec) Mean ± SD	Controls amplitude (mv.) Mean ± SD	P value
Right common peronieal	35.79±10.55	2.91 ± 1.75	50.46 ±7.74	3.40 ± 2.09	S.
Left common peronieal	34.76 ±12.58	1.46 ± 0.25	53.55 ± 9.71	3.23 ± 1.13	S.
Right posterior tibial	36.52±12.41	1.48 ± 0.24	50.33±6.90	2.87 ± 0.51	S.
Left posterior tibial	34.16±11.05	2.64±1.4	51.04±9.55	2.64±1.48	S.
Right sural	32.17 ± 10.4	1.72 ± 0.59	54.76 ±6.36	2.83 ± 0.60	S.
Lefttsural	34.33±10.65	1.72 ± 0.70	54.41 ± 7.17	2.93 ± 0.55	S.
Right median	44.09 ±7.04	2.42 ± 0.27	52.69±10.83	3.40 ± 0.31	S.
Left median	45.97 ± 9.36	1.46 ± 0.26	48.89 ± 8.47	3.09 ± 0.55	S.
Right ulnar	50.04 ± 7.63	3.12 ± 1.50	53.70 ± 5.06	3.45 ± 0.25	S.
Left ulnar	47.00 ± 3.30	3.19 ± 1.93	52.86 ± 4.91	3.41 ± 0.22	S.
Total	150	150	70	70	220

P<0.05, NS=non-significant , S =significant

Furthermore, there was a significant association between advancing age and longer-duration of diabetes with the reduction of conduction velocity and amplitude, as clarified in tables IV and V.

Table IV: Relationship between the age groups and impairment of nerve conduction in diabetic cases.

Age group (years)	Impaired Nerves conduction		Unimpaired Nerves conduction		Total
	No.	(%)	No.	(%)	
20-30	8	61.54	5	38.46	13
31-40	17	84.0	3	15	20
41-50	35	85.37	6	14.63	41
51-60	46	93.0	4	8	50
>60	25	96.15	1	3.85	26
Total	131	100	19	100	150

X2=10.874, p<0.05, S=Significant

Table V: Relation between the duration of diabetes and impaired nerves conduction in the diabetic patients.

Duration	Impaired Nerves conduction		Unimpaired Nerves conduction		Total
	Number	%	Number	%	
≤ 5years	15	75	5	25	20
6-10years	34	79.07	9	20.93	43
11-15	38	92.68	3	7.32	41
>15	44	95.65	2	4.35	46
Total	131	100	19	100	150

X2=9.343, P<0.05,S=Significant

Also, there is a significant inverse correlation between increased severity of diabetes disease (HbA1c level) and decreasing of both conduction velocity and amplitude, as shown in table VI.

Table VI: The relation of severity of diabetes and nerves conduction.

Severity of diabetes (HbA1c %)	Impaired Nerves conduction		Unimpaired Nerves conduction		Total
	Number	%	Number	%	
Mild HbA1c (≤ 7%)	16	80.00	4	20.00	20
Moderate HbA1c(8 - 9%)	38	84.44	7	15.5	45
Severe HbA1c (≥ 10%)	77	90.59	8	9.41	85
Total	131	100	19	100	150

X2=7.603, P<0.05, S =significant

However, the study demonstrated no statistical significant difference between patients and controls regarding the gender, as demonstrated in table VII.

Table VII: Relation between sex and impaired nerves conduction in diabetic patients.

	Impaired Nerves conduction		Unimpaired Nerves conduction		
Gender	No.	(%)	No.	(%)	Total
Male	82	88.71	11	11.83	93
Female	49	85.96	8	14.03	57
Total	131	100	19	100	150

X2=0.156, p>0.05, NS

Discussion

The study results showed a significant reduction ($p<0.05$) in both the nerve conduction velocity and amplitude of all examined nerves (common pernoeal, posterior tibial, sural, median and ulnar) from control to the diabetic patients. These findings were in agreements with that reported by other authors such as Kimura et al[8], Partanen et al[9], Ohkubo et al[10], Viswanathan et al[11], Younger et al[12], Pastore et al[13], Kohara et al[14], Vinik et al[15], Smith et al[16], Uluc et al[17], and Cermenati et al[18]. Nerve damage caused by Hyperglycemia by different mechanisms. Increasing the level of intracellular glucose with cellular toxicity in the endothelial cells of the capillaries related to peripheral nerves due to hyperglycemia[19]. This will lead to degeneration of myline sheath with reduction in the number of nerve fibres and alterations occurred in the endoneurial connective tissue, endoneurial vessels and perineurium[20]. A local nerve ischaemia could result from the abnormal vasa nervorum[21]. As a consequence the basement membrane of the endoneurial capillary is thickened and reduces the number of the tight junction between cells[22]. At first, conduction velocity reduces as a result of progression of nerve demylination then at the end will cause blocking of nerve conduction.

Another hypothesis participates in neuropathy by preventing normal axonal repair and regeneration due to effect of hyperglycemia that incites reduced formation of neurotropin like nerve growth factor (NGF)[19]. Furthermore, ischemia to the nerves which may contribute to neuropathy in hyperglycemia as a result of damage of the blood vessels which occurs because of conversion of intracellular glucose to what is called Amadori product, and these subsequently could form advanced glycosylated end products (AGEs),which cross-link matrix proteins[23].

In this study we found a correlation between nerve conduction defects and increasing age which represented by a significant decrease ($p<0.05$) in both nerve conduction velocity and amplitude with age advancing of diabetic patients in the studied sample. This finding in accordance with that reported by other authors like Albers et al[24], Viswanathan et al[11], Tesfaye et al[25], Ohgakio et al[26], and Loseth[27]. We could attribute the strong association between deterioration of nerve conduction velocity and amplitude with increasing age to the deleterious effects of long-term exposure to hyperglycaemia and lowering of the resistance of peripheral nerves as well as higher incidence of concomitant atherosclerosis leading to peripheral neuropathy.

Results of our study established a statistical significant correlation between the nerve conduction abnormalities and the increasing in duration of diabetes mellitus. The study showed that the most common affected group with decreasing of nerve conduction velocity and amplitude among all diabetic patients

groups in the studied sample was the group of the longer duration of the disease. This finding agrees with most other studies conducted about the nerve conduction changes in diabetic patients like Tesfaye et al[25], Barbosa et al[28], Rajbhandari and Piya[29], Janghorbani et al[30], Charles et al[31], and Malazy et al[32]. This is because of increased the chance of susceptibility to hyperglycemia deleterious complications with increase in the duration of the disease.

Electrophysiological findings established a strong negative impact of the severity of diabetes disease on the nerve conduction velocity and amplitude in the study sample. The study confirmed there was a statistical significant inverse correlation between HbA1c measurements(i.e the severity of diabetes) and the nerve conduction velocity and amplitude.

This study results was in accordance with that reported by other authors such as Vinik et al[15], Ohkubo et al[10], Viswanathan et al[11], and Charles et al[31].

Furthermore, glycemic control have an important role for the prevention of microvascular complications of diabetes and there is a strong association between the occurrence and progression of microvascular and macrovascular complications and hyperglycemia[33]. Hence, It is reasonable to conclude that a progressive neuronal involvement in the diabetic process which is accelerated by poor glycaemic control.

Regarding the gender effects, our electrophysiological measurements of both controls and diabetic patients in the study sample demonstrated that there was no significant statistical difference ($P>0.05$). This finding agrees with that reported by other studies such as Akbar et al[34], Loseth[27] and Charles et al[31]. However, our study disagrees with Mansour[35] who found that a percentage of women with nerve conduction abnormalities was significantly higher than that of men and Viswanathan et al[11] who claimed that nerve conduction impairment was significantly higher in men than women in his study. The explanation of these variations may be due to differences of methods, sample size, sex distribution of the sample and patient selection criteria.

In conclusion, the age of the patients, duration of the disease and the severity of diabetes (hyperglycemia control) are playing a crucial role as risk factors in impairment of nerve conduction and developing of peripheral neuropathy in diabetic patients.

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