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Original Research Article

The Duration of Type 2 Diabetes Mellitus as a Risk Factor For The Occurrence of Peripheral Neuropathy

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Abstract

This research was performed to evaluate type 2 diabetes mellitus duration as a risk factor for development of peripheral neuropathy (DPN).

Initially 157 patients with T2DM who fit the general inclusion criteria were collected, but only 61 of them enrolled in this study due to the application of restricted inclusion criteria and according to the results of the nerve conduction study (NCS) those 61 patients divided into two groups, group 1: 36 patients, had diabetic peripheral neuropathy (DPN), and group 2:25 patients without DPN. For all these patients a lot of investigations were performed to exclude any other cause of neuropathy(lipid profile, renal, thyroid functions, fasting blood sugar and glycated hemoglobin).

Significant statistical differences in the duration of T2DM between study groups was observed, p value was 0.04.The more duration of T2DM the high risk for diabetic peripheral neuropathy.

Key Words: Type 2 diabetes mellitus (T2DM), duration, diabetic peripheral neuropathy (DPN).

الخلاصة:

أجريت هذه الدراسة على المرضى المصابين بداء السكري من النوع الثاني, لتقييم تاثير زيادة المدة الزمنية لداء السكري على الاصابة باعتلال الأعصاب المحيطية (DPN). في البداية جمع 157شخص يعاني من مرض داء السكري النوع الثاني, ولكن فقط 61 منهم مسجلين في هذه الدراسة نتيجة لتطبيق المعايير المقيدة جدا على هؤلاء المرضى, ووفق النتائج دراسة التوصيل العصبي (NCS) فقد تم تقسيم هؤلاء المرضى الى مجموعتين, المجموعة 1: مكونة من 36 مريضا يعانون من اعتلال الأعصاب المحيطية (DPN)، والمجموعة 2: مكونة من 25 مريضا لا يعانون من اعتلال الاعصاب المحيطية (DPN) .لجميع هؤلاء المرضى أجريت الكثير من الفحوصات المختبرية لاستبعاد أي سبب الاعتلال العصبي تشمل (نسبة الدهون، وظائف الكلى، وظائف الغدة الدرقية، مستوى السكر في الدم في حالة الصيام ومستوى السكر التراكمي .

لوحظ في هذه الدراسة وجود فروق ذات دلالة إحصائية في مدة T2DM بين مجموعات الدراسة, وكانت قيمة احتمالي0.04.أكثر مدة لداء السكري T2DM تكون مصحوبة بمخاطر عالية لاعتلال الأعصاب المحيطية.

الكلمات المفتاحية: اعتلال الاعصاب المحيطية , داء السكزي النوع الثاني, مدة داء السكري.

Introduction

Type 2 diabetes mellitus result from combination of two mechanisms, the first one is progressive reduction in insulin secretion, and the second is development of resistance to insulin action, so the hyperglycemia that have been result is enough to cause pathological and functional changes in multiple body tissues, but with absence of any clinical manefestations and it may be present for a long time before diabetes is identify [1,2].

Diabetic neuropathy is one of chronic microvascular complications of DM present in both types of DM; T1DM and

T2DM that affect peripheral, somatic and autonomic nerves, it`s definition is the presence of symptoms and/or signs of peripheral nerve dysfunction in people with DM after the elimination of other causes of neuropathy [3,4]. It affects more than half of patients with T2DM [5].

Diabetic peripheral neuropathy (DPN) that as well called distal symmetric neuropathy or sensorimotor neuropathy is the most common form of diabetic neuropathy; the sensory distal lower extremities neuropathy is more predominant than motor and autonomic neuropath, although motor neuropathy occurs later in the course of the disease and whenever there is early motor affection the diagnostic severity of DPN increases [6].

Elevated glucose level in blood for long period is associated with enhancement of polyol pathway, increment of oxidative stress, elevation the non-enzymatic glycation of structural proteins, as well as alteration in protein kinase C activity and activation of poly ADP-ribose polymerase (PARP) that all harm endothelial tissue and creates changes that increases the resistance of the blood vessels and lessens blood current to the nerve with subsequent development of neuropathy [4,7].

Materials and Methods

In this case control study, initially 157 patients with T2DM who fit the general inclusion criteria were collected from centers of diabetic and endocrinology in Al-Sader and Merjan hospitals in Al-Najaf and Babylon cities, respectively. But with specific inclusion criteria, some of these patients had been excluded. The patient inclusion criteria and the details of the excluded cases are as follow:

-Their ages were ranged between 30-60 years.

- BMI range between 18.5-29.5 Kg/cm2.

- both gender were involved.

- they should had negative past medical history apart from DM.

-with no features suggestive other causes of neuropathy like nutritional deficiency, endocrine abnormality and others.

-they not utilized drugs like anti TB, lipid lowering agent or vitamin B supplementation.

-also there should be no any trauma throughout the whole length of tested nerves.

On applying these specific inclusion criteria, 91 patients were excluded because 56 of them were hypertensive, 23 patients had elevated lipid profile, 7 had abnormal thyroid function tests, 4 had history of ischemic heart disease and one patient had abnormal renal function test. From the remaining 66 patients that fit these inclusion criteria, 5 patients refuse to complete the nerve conduction study and hence omitted leaving only 61 patients to undergo the next procedures and statistics. The purpose of the research and the nature of the neurophysiological tests were explained to those patients and verbal consents were taken before the start of the tests.

All patients undergo a full clinical evaluation, including history taking according to well-prepared questionnaire, blood pressure measurement, body weight and height to calculate body mass index, if the history of the patients, their BMI and blood pressure fit to the specific inclusion criteria then after blood sample was taken to do the blood investigation (FBS, or RBS, HbA1c, renal function test, lipid profile and thyroid function test), then NCS is performed to evaluate the presence or absence of peripheral neuropathy by examining sensory and motor nerves in both upper and lower limbs, including ulnar, tibial, and sural nerves using Micromid electromyography device**.**

Those 61 T2DM patients were divided into two groups according to presence or absence of peripheral neuropathy that proved by electrophysiological study (NCS); Group 1 includes 36 patients with peripheral neuropathy, Group 2 includes 25 patients with no peripheral neuropathy.Diabetic patients are considered to have peripheral neuropathy

when at least one parameters(latancy, amplitude and conduction velocity) in at least 3 nerves in at least 3 limbs are abnormal [8,9].

Statistical analysis was done using SPSS v. 22 program, independent t test was used to test the level of significance (p-value), p value > 0.05 considered significant.

cut-off values:

- Fasting plasma glucose (FBG) ≥ 126 mg/dL (7.0 mmol/L) on two occasions, Glycated hemoglobin (Hb A1C) ≥ 6.5% [10].
- High density lipoprotein (HDL) < 40 mg/dl for men or 50 mg/dl for women, and abnormal Triglyceride (TRG) > 149 mg/dl considered abnormal[11].
- Systolic blood pressure of 135 mmHg or more and/or diastolic blood pressure 85 mmHg or more were categorized as having hypertention[12].

Results

Gender, age, systolic blood pressure (SBp), diastolic blood pressure (DBp), body mass index (BMI), fasting blood sugar (FBS), glycated hemoglobin (HbA1C),low-density lipoprotein cholesterol, triglyceride (TG), total cholesterol, high-density lipoprotein (HDL) cholesterol, blood urea, serum creatinine and thyroid function test (TSH) were analyzed and clarified in table 1.1. There was no significant statistical association between these risk factors and development of DPN (P > 0.05).

Table1: Distribution of study groups according to demographical and some clinical parameters

Parameter (mean ±SD)	patients with DPN	patients without DPN	P-value
Gender (male%)	58.3	52.0	0.7
Age (years)	50.4±6.5	47.6±7.0	0.1
BMI (kg\cm2)	24.3± 3.1	25.3 ± 2.0	0.2
SBp (mmHg)	116.0 ± 12.4	117.0 ± 14.0	0.9
DBp (mmHg)	69.1± 8.7	70.1± 15.5	0.2
HbA1c (%)	8.4 ± 1.4	8.3 ± 1.8	0.9
FBS(mg\dl)	223.5 ± 105.9	181.8 ± 91.9	0.1
TG (mg/dl)	155.8 ± 56.7	176.2 ± 67.2	0.6
Cholesterol (mg/dl)	152.0 ± 41.4	152.8 ± 30.7	0.4
HDL(mg/dl)	38.8±9.1	44.0±9.5	0.1
LDL(mg/dl)	112.3±23.9	102.5±26.8	0.5
TSH	1.2 ± 0.7	1.6 ± 1.3	0.5
B.urea (mg/dl)	53.3 ± 16.1	42.6 ± 18.4	0.8
S.createnin (mg/dl)	65.2 ± 6.0	65.4 ± 8.6	0.2

Regarding the duration of T2DM, the mean ±SD of duration in group 1 was 10.2 ±7.5 years, while in group 2 it was 6.6± 4.8 years, statistically, significant differences in the duration of T2DM between study groups was observed, p value was 0.04,as shown in figure (1.1).

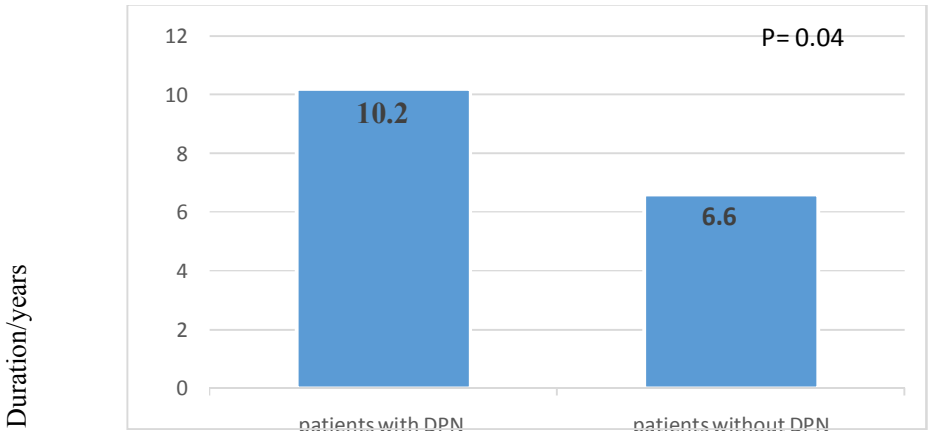

Figure 1: Distribution of study groups according to the duration of T2 DM.

Discussion

The results shows that diabetic patients with DPN have longer duration of diabetes with a significat difference from those without DPN (P=0.04). This may be explained by that persistent hyperglycemia for long period of time enhances polyol pathway, increases nonenzymatic glycation of structural proteins, stimulates the mitochondria to increase its formation of reactive oxygen species (ROS) as well as alters protein kinase C activity and poly ADP-ribose polymerase (PARP), all of these mechanisims are interrelated and result in harmful effect to the endothelial tissue and creates changes that increases the resistance of the blood vessels and lessens blood current to the nerve which will lead to development of neuropathy[4,7,13,14].

It seems simple,because when the duration of diabetes increases, the exposure to these pathogenic factors increases and the development of complications becomes more likely.

This result was consistent with results of many other researches that studied the relation between diabetic duration and DPN development [15,16,17,18] who demonstrated that the severity and confluence of DPN is increased as duration of diabetes is increased.

Moreover, Ghosal and coworkers 2012 verified that T2DM patients whom develop diabetic foot and had severe neuropathic and vascular disease have longer duration of diabetes when compared with those whom had shorter duration [19].

However, Haydari andhis study group and Kostev with his coworkers reported the presence of DPN in a given percent of newly diagnosed T2DM. This can be replied as many patients with T2DM might remain undiagnosed for many years during which hyperglycemia and subsequent metabolic, oxidative, neurovascular and other abnormalities are already present and causing their harmful effects on the tissues at the time of diagnosis [20, 21].

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