The Association of Low Taurine Levels with Diabetic Neuropathy in Iraqi Patients

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Abstract

Aim of this Study: this study has been carried out to evaluate the role of taurine, and lipid profile in progression of diabetic complication.

Methods: this work included 81 Iraqi people (age ranged 40-65). Healthy control subjects (G1 group=28), type 2 diabetes mellitus without any complications (G2 group=26), and type 2 diabetes mellitus with peripheral neuropathy (DPN) (G3 group=27). Diagnosis of the disease was based on several symptoms and questions under the supervision of the consultant supervisor at the center. Serum taurine, lipid profile (Cholesterol, triglycerides, HDL, LDL, and VLDL) besides fasting blood glucose and plasma HbA1c were determined for each participant. **Results:** The results of taurine revealed that there was a highly significant decrease in G2 and G3, as compared to G1. The mean values of serum cholesterol showed no significant difference between G2 and G3 as compared with G1while serum triglycerides (TG), LDL and VLDL showed a high significant increase in G2 and G3 as compared to G1. The results of serum HDL levels showed that there was a high significant decrease in G2 and G3 as compared to G1. No significant differences were found in body mass indices in all the studied groups while WC, HC, WHR, and WHtR showed high significant increase in G2and G3 as compared to G1. Systolic blood pressure significantly increased in G2 and G3 while diastolic blood pressure significantly increased in G3 only.

Conclusion: Serum taurine levels were decreased in patients with T2DM and DPN .The reducing in taurine synthesis was not related to FBG, HbA1c, and dyslipidemia. We also found that taurine levels may be more important in the development of diabetes complications.

Keywords: *Type 2 DM, diabetic peripheral neuropathy, taurine, dyslipidemia.*

Introduction

Diabetes mellitus is a heterogeneous metabolic disorder that is characterized by the presence of hyperglycemia that happened due to impairment of defective insulin action, insulin secretion, or may be both. The chronic hyperglycemia of diabetes mellitus is correlated with long term microvascular complications affecting the nerves, eyes, kidneys, as well as an increased risk for cardiovascular disease (CVD)[1].Type 2 diabetes is a serious and common chronic endocrine disorder with risk factors such as obesity and sedentary lifestyle that is constitute a major worldwide public health [2]. The interaction between some of genetic and environmental factors results in a heterogeneous and progressive disorder with variable degrees of beta cell dysfunctions and insulin resistance. The β cells when have no longer ability to secrete sufficient insulin to overcome insulin resistance, impaired glucose tolerance progresses to type-2 diabetes[3]. Diabetic peripheral neuropathy (DPN) is one of the most known chronic complications of type two diabetes and is defined as a neurological damage in patients with diabetes mellitus and it is a condition where blood supply to nerves in the feet or hands is impaired causing the nerve to malfunction and eventually die out and its cause burning pain, aching or numbness, pins and needles sensation. It affects 30% - 50% of diabetic patients .Taurine (2-aminoethanesulfonic acid) is essential naturally occurring beta-sulphonated amino acid which is not utilized in protein synthesis and never incorporated into muscle proteins, so it's found as a free molecule in the body or as simple peptides along with methionine and cysteine [4]. Increasing evidence suggested that taurine might play a role in improving DPN because of its ability to prevent SCs apoptosis. The main pathological feature of diabetic peripheral neuropathy is myelin sheath damage of peripheral nerve that was accelerated by schwann cells (SCs) apoptosis[5]. A recent study confirmed that taurine significantly lowers the blood glucose levels, reduces insulin resistance and dysfunctional nerve condition in diabetic mice[6]. Lipid abnormalities are commonly found in patients with diabetes mellitus, this abnormality called dyslipidemia which is one of the major risk factors that's leads to cardiovascular disease in diabetes mellitus. The characteristic features in lipid of diabetic patients with type two are a high plasma triglyceride concentration, low HDL cholesterol concentration and increased concentration of small dense LDL-cholesterol particles[7], [8]. Cholesterol is one of the lipids and major sterol in animals, is both precursor to a wide variety of steroids and structural component of membranes. It is an essential component of the cellular membranes determining the fluidity and biophysical properties by increasing the compactness and lowering the permeability. It is also a source of bioactive molecules such as vitamin D, bile acids and steroid hormones [9]. Taurine changes the abnormal blood lipid profile that is associated with the diabetic condition. It was proved that elevated plasma triglycerides and LDL cholesterol in diabetics were lowered through administration of taurine [10]. Taurine negatively affects lipid levels by reducing lecithin cholesterol acyltransferase activity [11]. Taurine significantly reduced both resting systolic and diastolic blood pressure and these finding indicate that taurine can reduce the incidence of CVD by ~ 6% in both hypertensive and normotensive individuals [12], [13] .

Materials and Methods

Study groups include 28 control subjects (G1) and 53 Iraqi patients with type 2 diabetes(age from 40-65) and the patients classified into two subgroup: group (G2) (with a duration 2-8 years) including patients with type 2 diabetes without complication (T2DM) and group (G3) (with a duration 2-10 years) including patients with type 2 diabetes with peripheral neuropathy complication (DPN) .The patients enrolled in the study were attending to National Diabetes Center/ Al-Mustansiriya University during the period from December 2019 to march 2020 under the supervision of Dr. Firas younus Muhsin. Diagnostic criteria for the patients based on the American

Diabetes Association (ADA) (FBG≥ 126 mg/dL, plasma glucose≥200 and HbA1C≥6.5%) [14]. In this study we excluded patients with type one diabetic patients, type two diabetic patients who are taking insulin as a hypoglycemic therapy, nephropathy and retinopathy, patients with cardiovascular disease and those having liver diseases and other known diseases which are associated with glucose metabolism disordered. The control group was matched with the patients' groups in age, BMI and gender.

Methods

Blood samples were obtained by venipuncture from each individual about five ml after (10-12) hours of fasting. The blood sample was divided into two portions; 2 and 3 ml. The first portion was dispensed in tube containing ethylene diamine tetra acetic acid (EDTA) which used for the estimation of HbA1C. While the second portion was dispensed in a gel tube and left to clot at room temperature. The gel tube was centrifuged at (3000 r.p.m) for 10 minutes to collect serum which is used for estimation taurine, lipid profile (Cholesterol, TG, and HDL). Taurine was measured by using enzyme linked immunosorbent assay (ELISA) using the commercially available ELISA kit (Mybiosource, U.S.A). All procedures were carried out according to the manufacturer's instructions, Cholesterol (HUMAN, Germany), Triglycerides (TG) (HUMAN, Germany), and HDL (HUMAN, Germany). LDL was calculated from this equation: LDL-C= [Cholesterol - (T.G. /5) - HDL-C]. VLDL was calculated from this equation: VLDL-C (mg/dl) = Triglyceride/5 [15].

Statistical Analysis

The data was statistically analyzed by SPSS software program version 22. The variables were reported as means ± standard deviation. The groups were compared by using one-way ANOVA and post hoc Tukey test, with a P value of <0.05 indicating the statistically significant difference.

Results

The results of our study presented in Table (1) revealed that fasting blood glucose (FBG) showed a high significant increase (p=0.000) in G2 (154.38±50.61 mg/dl) and G3 (220.88±91.58mg/dl) as compared to G1(86.61±5.12mg/dl), while G2 (p=0.000) showed a highly significant decrease as compared to G3(154.38±50.61mg/dl vs. 220.88±91.58mg/dl).For HbA1c the results showed a high significant increase (p=0.000) in G2(8.09±1.29 %) and G3 (8.72±1.86 %) as compared to G1 (4.82±0.56 %) ,while there was no significant different (p=0.210) between G2 and G3

The results found in Table (1) revealed that the mean values of Taurine levels showed highly significant decrease (p=0.000) in G2 (1.78 ± 1.26ng/ml) and G3(1.55±1.99ng/ml) as compared to G1(3.13±0.64ng/ml). While, there was no significant between (G2) (p=0.818) and (G3) (1.78±1.26ng/ml vs. 1.55±1.99ng/ml).

The mean values of serum cholesterol showed no significant differences between G2 (182.77±38.66 mg/dl, p=0.059) and G3(178.22±40.17 mg/dl, p=0.160) as compared to G1 (161.10±21.48mg/dl), also there were no significant differences (p=0.880) between G2 and G3. For serum triglycerides (TGs) the results showed a high significant increase in G2 as compared to G1 (246.46±150.33 mg/dl, p=0.000) and in G3 (217.44±79.65 mg/dl, p=0.003) as compared to G1(128.68± 12.05 mg/dl) and there was no significant difference (p=0.524) between G3 and G2. HDL levels showed a high significant decrease in G2 (41.29±7.34 mg/dl, p=0.000) and in G3 (40.38±6.93 mg/dl, p=0.000) as compared to G1(57.57± 11.92 mg/dl) and there was no significant difference (p=0.929) between G3 and G2.

Table 1: The characteristics of participants FBG, HbA1c, Taurine, Cholesterol, TG, HDL, LDL, VLDL among different groups (n=81).

Variables	G1 (Mean±SD) Control N=28	G2 (Mean±SD) T2DM N=26	G2 (Mean±SD) DPN N=27	p-value	
FBG (mg/dl)	86.61±5.12	154.38±50.61	220.88±91.58	G1*G2	0.000**
				G1*G3	0.000**
				G2*G3	0.000**
HbA1c (%)	4.82±0.56	8.09±1.29	8.72±1.86	G1*G2	0.000**
				G1*G3	0.000**
				G2*G3	0.210
Taurine(ng/ml)	3.13±0.64	1.78±1.26	1.55±1.99	G1*G2	0.002*
				G1*G3	0.000**
				G2*G3	0.818
Cholesterol(mg/dl	161.10±21.48	182.77±38.66	178.22±40.17	G1*G2	0.059
				G1*G3	0.160
				G2*G3	0.880
TG (mg/dl)	128.68± 12.05	246.46±150.33	217.44±79.65	G1*G2	0.000**
				G1*G3	0.003**
				G2*G3	0.524
HDL(mg/dl)	57.57± 11.92	40.38±6.93	41.29±7.34	G1*G2	0.000**
				G1*G3	0.000**
				G2*G3	0.929
LDL(mg/dl)	78.64±21.94	100.62±35.94	100.15±36.84	G1*G2	0.037*
				G1*G3	0.040*
				G2*G3	0.998
VLDL(mg/dl)	25.76±2.51	46.95±29.89	43.43±15.68	G1*G2	0.000**
				G1*G3	0.003**
				G2*G3	0.784

A high significant increase was found in LDL levels of G2 (100.62±35.94 mg/dl, p=0.000) and of G3(100.15±36.84 mg/dl, p=0.000) as compared to G1(78.64±21.94 mg/dl) but there was no significant difference (p=0.998) between G2 and G3. Serum VLDL showed a high significant increase in G2 (46.95±29.89, p=0.000) and G3 (43.43±15.68 p=0.003) as compared to G1 (25.76±2.51 mg/dl), but there was no significant difference (p=0.784) between G3 and G2.

Table (2) showed the results of anthropometric measurements and indicated that BMI had no significant difference between G2 (30.62±6.33 kg/m^2, p=0.490), and G3 (32.26±6.47 kg/m2, p=0.078) as compared to G1(28.79±4.63 kg/m2), either there were no significant differences

(p=0.564) between G2 and G3. For the waist circumference (WC) the results showed a high significant increase in G2 (109.54±9.51 cm, p=0.000) and G3 (111.11±11.05 cm, p=0.000) as compared to G1 (96.21±14.75 cm), but there were no significant differences between G2 and G3 (p=0.883). The hip circumference (HC) results showed that there were no significant differences between G1 (p=0.173) and G2 (110.39±12.67cm vs. 116.15±9.84 cm), but a significant increase in G3 (p= 0.034) was found as compared to G1 (118.41±12.25 cm vs. 110.39±12.67 cm), also there were no significant differences (p=0.763) between G2 and G3. The obtained results of WHR in G2 (0.94±0.03) and G3 (0.94±.074) showed a highly significant increase (p=0.003) as compared to G1 (0.87±0.09) but there was no significant difference (p=0.997) between G2 and G3. The results of WtHR showed a highly significant increase in G2 (0.69±0.095, p=0.000) and G3 (0.67±0.083, p=0.001) as compared to G1 (0.58±0.076) but there was no significant difference (p=0.545) between G2 and G3.

Table 2: The characteristics of anthropometric measurements among different groups (n=81).

Variables	G1 (Mean±SD) Control N=28	G2 (Mean±SD) T2DM N=26	G2 (Mean±SD) DPN N=27	p-value	
BMI(kg/m2)	28.79±4.63	30.62±6.33	32.26±6.47	G1*G2	0.490
				G1*G3	0.078
				G2*G3	0.564
WC(cm)	96.21±14.75	109.54±9.51	111.11±11.05	G1*G2	0.000**
				G1*G3	0.000**
				G2*G3	0.883
HC(cm)	110.39±12.67	116.15±9.84	118.41±12.25	G1*G2	0.173
				G1*G3	0.034*
				G2*G3	0.763

Cont... **Table 2: The characteristics of anthropometric measurements among different groups (n=81).**

WHR	0.87±0.09	0.94±0.03	0.94±.074	G1*G2	0.003*
				G1*G3	0.003*
				G2*G3	0.997
WtHR	0.58±0.076	0.69±0.095	0.67±0.083	G1*G2	0.000**
				G1*G3	0.001**
				G2*G3	0.545
SBP (mmHg)	120±1.90	144.07±21.98	147.59±28.75	G1*G2	0.000**
				G1*G3	0.000**
				G2*G3	0.812
DBP (mmHg)	79.92 ± 2.01	85.23± 13.37	94.74±16.21	G1*G2	0.248
				G1*G3	0.000**
				G2*G3	0.015*

The SBP results showed that there was a highly significant increase in G2 (144.07±21.98 mmHg, p=0.000) also in G3 (147.59±28.75 mmHg, p=0.000) as compared to G1 (120±1.90 mmHg) but there was no significant difference (p=0.812) between G2 and G3. The DBP results showed no significant difference (p=0.248) between G1 and G2 (79.92 ± 2.01 mmHg vs. 85.23± 13.37mmHg).

While there was a highly significant increase in G3 (p=0.000) as compared to G1 (94.74±16.21 mmHg vs. 79.92 ± 2.01 mmHg). In addition a highly significant decrease (p=0.013) was found in G2 as compared to G3 (85.23± 13.37 mmHg vs. 94.74±16.21 mmHg).

Table (3): Pearson correlation of Taurine in (G2) and (G3) groups.

parameters	**Taurine(ng/ml)**			
	G2 (T2DM group)		**G3 (DPN group)**	
	r	**p**	**r**	**p**
FBG (mg/dl)	-0.059	0.773	-0.063	0.754
Hba1c (%)	0.163	0.426	-0.106	0.599

***Cont...* Table (3): Pearson correlation of Taurine in (G2) and (G3) groups.**

Cholesterol(mg/dl)	0.083	0.688	-0.394	0.042*
TG (mg/dl)	-0.235	0.247	0.012	0.955
HDL (mg/dl)	-0.042	0.839	-0.034	0.867
LDL (mg/dl)	0.148	0.469	-0.379	0.051
VLDL	-0.341	0.088	0.018	0.928
BMI (kg/m2)	0.045	0.827	-0.029	0.884
WC (cm)	-0.491	0.011*	-0.031	0.878
HC (cm)	-0.509	0.008**	-0.034	0.868
WHR	0.069	0.738	-0.021	0.917
WtHR	0.212	0.298	0.020	0.921
SBP (mm/Hg)	-0.234	0.250	0.063	0.755
DBP (mm/Hg)	-0.305	0.130	0.039	0.846

R, Pearson coefficient

***Statistically significant at $p \leqslant 0.05$**

Table (3) showed the correlations of serum Taurine with other biochemical parameters in Type 2 diabetes mellitus (G2) and diabetic peripheral neuropathy (G3). The results showed that Taurine was correlated negatively in G2 with WC (r= -0.491, p=0.011) and also, a highly negative correlation was found with HC (r= -0.509, p=0.008). Taurine had a negative correlation with cholesterol in G3 (r= -0.394, p=0.042). While there was no correlation relationship between taurine and other parameters in G2 and G3 respectively.

Conclusion

Serum taurine levels were decreased in patients with T2DM and this was not correlated with FBG, HbA1c, and dyslipidemia. Also, we found an inverse correlation between taurine with waist (WC) and hip (HC) circumference associated with increasing systolic and diastolic blood pressure, we think taurine can be used to predict the progression of diabetes in obese subjects considering the elevated cardiometabolic risk.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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