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Effects of Diet Treatment on Some Biochemical and Physiological Parameters in Patients with Type 2 Diabetes Mellitus

ISMAIL MERAL and RACI KACMAZ[1]

Department of Physiology, Veterinary Medicine, Yuzuncu Yil University, [1]*Biochemistry Laboratory, Social Insurance Hospital, Van, Turkey*

MERAL, I. and KACMAZ, R. *Effects of Diet Treatment on Some Biochemical and Physiological Parameters in Patients with Type 2 Diabetes Mellitus.* Tohoku J. Exp. Med., 2003, **200** (1), 25–30 —— The aim of the present study was to investigate the effect of diet treatment on serum glucose, triglyceride (TG), total cholesterol (TC), high density lipoprotein-(HDL) cholesterol, low density lipoprotein-(LDL) cholesterol and very low density lipoprotein-(VLDL) cholesterol levels, systolic and diastolic blood pressure and electrocardiograms (ECGs) in patients with type 2 diabetes mellitus (DM). Twenty healthy subjects (mean age 45.9±3.7 years) and newly diagnosed patients with type 2 diabetes prior to receiving diet treatment (mean age 47.6±6.2 years) were included in this study. Diabetic patients were given a standard dietary treatment that was composed of 50% to 55% carbonhydrate and 30% fat (1200 kcal for women and 1600 kcal for men) for 2 months. No diet treatment was applied for control. For both groups serum glucose, TG, TC, HDL-cholesterol, LDL-cholesterol and VLDL-cholesterol levels, systolic and diastolic blood pressure and ECGs were measured at the beginning and end of the diet treatment. Although diet treatment decreased the elevated serum glucose in diabetic patients, it still remained higher than that in the controls. Diet treatment also decreased the elevated TG and VLDL-cholesterol in diabetic patients to control values. Although heart rate and systolic blood pressure were higher, diastolic blood pressure was not different in diabetic patients than those in controls. Ventricular hypertrophy was also observed in ECGs of 10% of diabetic patients. Diet treatment normalized all of these findings, except systolic blood pressure. This study showed that diet treatment could not normalize the high systolic blood pressure in type 2 DM. Thus, an effective way of controlling blood pressure should be taken to improve healing in DM. ———— diabetes mellitus; ECGs; triglyceride; hypertension; diet treatment

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Address for reprints: Ismail Meral, Ph.D., Yuzuncu Yil Universitesi, Veteriner Fakultesi, Fizyoloji Anabilim Dali, 65080, Kampus, Van, Turkey.

e-mail: imeral20@hotmail.com

Insulin deficiency, resistance to the action of insulin or both leads to the development of diabetes mellitus (DM). About 90% of people with DM have non-insulin-dependent (type 2) DM, while the other 10% have insulin-dependent (type 1) DM (Granner 1993). Type 2 DM leads to abnormalities in carbohydrate, protein and lipid metabolism, and increases the risk of developing atherosclerotic arterial disease by two- to six fold (Sacks 1997; Sekeroglu et al. 2001). It has been suggested that atherogenic risk factors such as total cholesterol (TC), very low density lipoprotein-(VLDL) cholesterol, triglyceride (TG) and uric acid increase in type 2 diabetes (Yenigun 1997; Palmieri et al. 2001). It has been also suggested that heart rate, systolic blood pressure, pulse pressure, left ventricular mass and its relative wall thickness are higher in type 2 diabetes than in non-diabetic individuals (Palmieri et al. 2001). In long-term, cardiomyopathy and congestive heart failure may also develop as a result of impaired left ventricular function (Ozturk et al. 1998).

Most studies regarding DM have investigated the complications in type 2 diabetic patients with no treatment and demonstrated that many systems including cardiovascular and gastro-intestinal systems have been affected in the body (Ozturk et al. 1998). It has been suggested that some complications of DM including high serum glucose and TG concentrations could be normalized by diet treatment (Goldberg 1981; Pinar 1998). But there is no information whether diet treatment could also normalize the some cardiovascular complications of diabetic patients. Thus, this study was designed to investigate the effects of diet treatment on serum glucose, TG, TC, high density lipoprotein-(HDL) cholesterol, low density lipoprotein-(LDL) cholesterol and VLDL-cholesterol levels, systolic and diastolic blood pressure and electrocardiograms (ECGs) in patients with type 2 DM.

Materials and Methods

Two study groups; control and newly diagnosed untreated-type 2 DM were included. The patients were admitted to the Social Insurance Hospital (Van, Turkey) and diagnosed of type 2 diabetes with fasting plasma glucose $\geqq$ 126 mg/100 ml (7 mmol/liter) were accepted as diabetics (Sekeroglu et al. 2001). The diagnosis was confirmed after oral glucose tolerance test. Twenty patients were selected consecutively to represent newly diagnosed untreated-type 2 diabetic patients. These patients underwent standard dietary treatment for 2 months to bring their weight back to ideal limits. The diet was composed of 50–55% carbohydrate and 30% fat (1200 kcal for women and 1600 kcal for men). None of the patients had ketoacidosis or had taken hypolipidemic drug. No diet or drug treatment was applied to control group. Twenty healthy individuals served as control group matched for age, sex, body mass index (BMI) and smoking status were selected from hospital staff and other outpatients clinics. The characteristics of control subjects, and type 2 patients are given in Table 1.

The study protocol was followed only after obtaining the voluntary consents of the subjects. A full explanation of the study protocol was given to the subjects before their consents were requested. The patients received care accord-

Table 1. *Characteristics of diabetic patients and control subjects (Mean±S.D.)*

	Controls (n=20)	Diabetic Patients (n=20)
Age (year)	47.6±6.2	51.1±6.4
BMI (kg/m^2), before-after the study	28.4±3.2–28.6±4.1	27.9±2.2–26.7±1.51
Sex (male: female)	9 : 11	11 : 9
Smoking (smokers: non-smokers)	8 : 12	8 : 12

ing to the criteria outlined in the Ethics of the World Medical Association (WMA Declaration 2000).

Blood samples were drawn after an overnight fasting in all groups before and after the study. Glucose was determined in the serum samples by routine methods using glucose oxidase on a Technicon DAX-24 (Technicon Ltd., Swords Co., Dublin, Ireland) autoanalyser (Yenson 1986). An automated enzymatic colorimetric method by using commercial kits (Bayer, Germany) was performed for the serum TG, TC and HDL-cholesterol determinations on the Technicon DAX-24 autoanalyser (Technicon DAX System Methods Manual 1994). Serum LDL- and VLDL-cholesterol levels were calculated according to the method described by Friedewald et al. (1972).

ECGs were recorded by a direct writing electrocardiograph (Cardiofax 02611; Nihon Kohden, Tokyo). All ECGs were standardized at 1 mV=10 mm, with a chart speed of 25 mm/sec. Leads I, II, III, aVR, aVL, aVF, V1, V2, V3, V4, V5 and V6 were recorded before the blood withdrawal. Heart rate, and the durations and amplitudes of waves on the trace were measured in lead II (Little and Little 1989). Systolic and diastolic blood pressures in the brachial artery were also measured indirectly with the aid of a special sphygmomanometer (Erkameter 3000, Chemnitz, Germany) before the blood withdrawal (Little and Little 1989).

The data were expressed as mean with standard deviation (S.D.). Student's t-test was used to compare patients vs. control subjects pre- and post-diet treatment. The paired t-test was used to compare values before and after 2-month intervention period.

RESULTS

Table 2 shows pre- and post-diet treatment results of serum glucose, TC, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol and TG levels in patient and control groups. Because control values were almost the same before and after the 2-month experimental period, only parameters obtained form control subjects after the 2-month experimental period are shown. Glucose level was significantly higher ($p<0.05$) in diabetic patients in both treated and untreated groups. Diet treatment decreased the elevated glucose level in patients significantly ($p<0.05$) compared to the untreated diabetic patients. However, glucose level in the treated group was still higher ($p<0.05$) than those in controls. The TG and VLDL-cholesterol levels of the untreated diabetic patients were significantly higher ($p<0.05$) than those in controls. However, diet treatment decreased the elevated TG and VLDL-cholesterol levels of diabetic patients to the control levels. There was no difference in the TC, HDL-cholesterol and LDL-cholesterol, among the groups.

Amplitudes and durations of waves, heart rates and blood pressures of diabetic patients and controls before and after diet treatment are

TABLE 2. *Biochemical parameters of diabetic patients and controls before and after diet treatment (Mean±S.D.)*

Parameters (mg/100 ml)	Controls ($n=20$)	Diabetic patients before dietary treatment ($n=20$)	Diabetic patients after dietary treatment ($n=20$)
Glucose	86.9±3.0[a]	348.6±27.7[b]	169.4±11.1[c]
Total cholesterol	212.9±12.6	231.9±16.9	227.2±17.7
HDL-cholesterol	40.4±1.6	44.4±2.0	40.2±1.5
LDL-cholesterol	130.4±13.1	139.4±10.4	150.9±13.9
VLDL-cholesterol	40.2±6.3[a]	60.1±11.6[b]	38.4±3.6[a]
Triglyceride	201.2±31.9[a]	290.0±58.2[b]	192.4±18.4[a]

[a,b,c]: Means in the same column with different superscripts significantly differ ($p<0.05$).

TABLE 3. *Amplitudes and durations of waves, heart rates and blood pressures of diabetic patients and controls before and after diet treatment (Mean±S.D.)*

Parameters	Controls ($n=20$)	Diabetic patients before dietary treatment ($n=20$)	Diabetic patients after dietary treatment ($n=20$)
Waves			
P (seconds)	0.040 ± 0.003^{a}	0.080 ± 0.007^{b}	0.070 ± 0.007^{b}
P (mv)	0.10 ± 0.03	0.13 ± 0.04	0.10 ± 0.02
QRS (seconds)	0.060 ± 0.008	0.060 ± 0.009	0.050 ± 0.006
QRS (mV)	0.55 ± 0.04	0.70 ± 0.07	0.70 ± 0.07
T (seconds)	0.14 ± 0.03	0.12 ± 0.03	0.18 ± 0.03
T (mV)	0.25 ± 0.04	0.20 ± 0.04	0.25 ± 0.05
P-Q (seconds)	0.20 ± 0.03	0.16 ± 0.04	0.16 ± 0.04
Q-T (seconds)	0.16 ± 0.02	0.16 ± 0.02	0.18 ± 0.02
Heart rate (beats/minutes)	76.9 ± 8.2^{a}	105.1 ± 11.4^{b}	67.3 ± 12.6^{a}
Blood pressure (mm-Hg)			
Systolic	117.0 ± 13.8^{a}	114.0 ± 23.8^{b}	139.0 ± 22.4^{b}
Diastolic	76.0 ± 9.8	87.0 ± 17.8	85.0 ± 11.9

[a,b]: Means in the same column with different superscripts significantly differ ($p<0.05$).

shown in Table 3. These readings are the representatives of the majority of subjects. Similar to biochemical findings because control values were almost the same before and after the 2-month experimental period, only parameters obtained form control subjects after the 2-month experimental period are shown. In control group, P wave was negative in lead aVR and positive in other leads. The mean duration of P wave was 0.040 ± 0.003 seconds and its mean average amplitude was 0.10 ± 0.03 mV. Q wave was only seen in leads I, aVL, V1, V2, V3, V4, V5 and V6. The mean duration of QRS complex was 0.060 ± 0.008 seconds and its mean average amplitude was 0.55 ± 0.04 mV. T wave was negative in leads aVR and V1, and positive in other leads. The mean duration of T wave was 0.14 ± 0.03 seconds and its mean average amplitude was 0.25 ± 0.04 mV. The heart rates of control subjects were 78.94 ± 8.25 beats/minutes. It was found that the mean duration of P wave increased ($p<0.05$) in the both patient groups. Although heart rate increased ($p<0.05$) in untreated patients with type 2 DM, it decreased to control level in the treated group. Although mean electrical axis was $+85\pm9.3^{\circ}$ in control group, it decreased ($p<0.05$) to $+71\pm8.6^{\circ}$ in the untreated patients group. The mean electrical axis $+75\pm7.7^{\circ}$ in the patients on treatment was still lower ($p<0.05$) than those in control group.

Systolic and diastolic blood pressures of control subjects, patients with type 2 DM untreated and with type 2 DM treated groups are shown in Table 3. Although systolic blood pressure increased ($p<0.05$), diastolic blood pressure did not change in untreated type 2 diabetic group. Diet treatment did not decrease ($p<0.05$) the elevated systolic blood pressure of diabetic patients.

DISCUSSION

The results of the present study indicated that diet treatment significantly decreased the elevated glucose level of diabetic patients. It has been suggested that diet treatment decreases the resistance to the insulin-dependent glucose uptake causing an increase in glucose transport into the cells with a consequent decrease in serum glucose concentration (Pinar

1998). Diet treatment did not decrease the glucose level to the control level in our study. This indicates persistence of resistance to the insulin action with or without circulating insulin in the body despite the diet and antidiabetic drug treatment.

Diet treatment also decreased the elevated TG and VLDL-cholesterol levels of diabetic patients to the control level in the present study. Our finding is consistent with those of other researchers (Goldberg 1981; Ferri et al. 1999). It has been suggested that increase in VLDL-cholesterol and TG levels in type 2 diabetic patients was due to the resistance to insulin-dependent glucose uptake which increases the serum glucose concentration, leading an increase in hepatic VLDL-cholesterol and TG synthesis and secretion (Reaven and Mondon 1984; Reaven 1988). Thus, VLDL-cholesterol and TG secretion is related to the serum glucose concentration. This also explains the normalized VLDL-cholesterol and TG level in diet drug treated patients who have lowered glucose concentration.

The heart rate and systolic blood pressure increased, diastolic blood pressure did not change in untreated patients with type 2 diabetes. Our results were consistent with the results of some other researchers who showed an increase in systolic blood pressure and heart rate, and impaired left ventricular function in type 2 diabetic patients (Claudi et al. 2000; DeSimone et al. 2000). It has been suggested that there is a relationship between the hypertension, insulin resistance and DM (Palmieri et al. 2001). Patients with type 2 diabetes had higher systolic blood pressure, pulse pressure and heart rate (Palmieri et al. 2001). Left ventricular mass and relative wall thickness were also higher in diabetic than non-diabetic subjects (Palmieri et al. 2001). DeSimone et al. (2000) investigated the cardiac abnormalities in diabetic patients and found that patients had higher systolic blood pressure and left ventricular dimension. In long-term diabetes, cardiomyopathy and congestive heart failure may develop as a result of impaired left ventricular function (Ozturk et al. 1998). We did not observe any cardiomyopathy or congestive heart failure in the present study probably due to shorter duration of diabetes in the newly diagnosed untreated patient group. Although diet treatment normalized the heart rate, left ventricular function and mean electrical axis of diabetic patients, it did not decrease the elevated systolic blood pressure. Similar to our result, Kjeldsen et al. (2000) suggested that diabetic patients needed more medication than non-diabetic patients to gain blood pressure control. They also emphasized the need for two or more drugs to control high blood pressure in most of these patients. Thus, diet treatment alone might not be enough to decrease the elevated systolic blood pressure in diabetic patients.

It was concluded that some of the complications occured in DM could be normalized by diet treatment. However, DM is associated with less blood pressure response despite the diet treatment. Thus, to be able to get better results in the treatment of diabetic patients, an effective way of controlling high blood pressure should be considered. However, two months of dietary treatment might be too short to demonstrate the blood pressure response of diabetic patients. Therefore, more studies with longer time of dietary treatment are needed to evaluate the blood pressure changes in DM.

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