Serum Lipoprotein(a) is Increased in Hypertensive NIDDM Patients

Contrasting data are available in the literature regarding lipoprotein(a) [Lp(a)] and coronary heart disease (CHD) in diabetic patients (1,2,3). Because hypertension (HT) is a risk factor for cardiovascular disease in diabetic patients (4), we wanted to assess whether Lp(a) concentrations differ in hypertensive versus normotensive non-insulin-dependent diabetes mellitus (NIDDM) patients.

Eighty-nine NIDDM patients were studied, and 30 healthy volunteers served as control subjects. Blood pressure (BP) was determined using a random zero sphygmomanometer, and HT was diagnosed when BP was higher than 140/90 mmHg on three different occasions or when an antihypertensive medication was prescribed to a patient (5). No significant differences in age, sex, duration of illness, blood glucose, HbA_1, or total cholesterol, high-density lipoprotein cholesterol, and triglyceride levels were present between normotensive and hypertensive NIDDM patients (Table 1). The prevalence of diabetic retinopathy, neuropathy, and nephropathy did not differ between the two groups. Because there are reports arguing that levels of Lp(a) are increased in NIDDM patients with CHD (1) and the association between CHD and HT is often present, we divided the hypertensive NIDDM patients into two subgroups: with CHD and without CHD. A definite history of angina was confirmed by a physician, and a history of myocardial infarction (MI) was documented by electrocardiographic changes. Lp(a) levels were determined using a commercially available enzyme-linked immunosorbent assay kit (Boehringer-Mannheim, Germany) with a detection limit of 0.05 mg/dl. Lp(a) values are given as medians and ranges, and Mann-Whitney *U* test was used to compare Lp(a) concentrations between the groups. Correlation analysis was done using Spearman's rank correlation.

Table 1—*Clinical and metabolic characteristics of NIDDM patients with or without HT*

	NIDDM patients		
	Normotensive	Hypertensive	*P* value
n	30	59	—
Age (years)	54 (33–69)	57 (35–66)	NS
Sex (M/F)	13/17	28/31	NS
Duration of illness (years)	9.4 (1–27)	8.9 (1–25)	NS
Glycemia (mg/dl)	267.7 ± 100.0	293.1 ± 93.8	NS
HbA_1 (%)	8.3 ± 2.4	9.2 ± 1.9	NS
Total cholesterol (mg/dl)	230.0 ± 51.4	221.0 ± 61.1	NS
HDL = High-density lipoprotein cholesterol (mg/dl)	44.1 ± 9.05	43.5 ± 8.2	NS
Triglycerides (mg/dl)	125.9 ± 28.8	117.7 ± 46.1	NS
Having CHD (%)	20.0	69.4	0.012
Lp(a) (mg/dl)	1.1 (0.05–9.6)	3.9 (0.05–203.7)	<0.005
Lp(a) >30 mg/dl (%)	0.0	16.9	0.027

Data are given as means ± SD or median (range).

Of the 89 NIDDM patients, 30 were normotensive and 59 had HT. No difference in Lp(a) concentration was observed between healthy volunteers (1.6 mg/dl [0.05–138]) and normotensive NIDDM patients (1.1 mg/dl [0.05–9.6], $P > 0.05$). Compared with normotensive NIDDM subjects, the patients with HT had a significantly increased Lp(a) concentration (3.9 mg/dl [0.05–203.7], $P < 0.005$). When divided, the hypertensive patients without CHD had similar Lp(a) concentrations (4.4 mg/dl [0.05–203.7]) to those in patients with HT and CHD (3.6 mg/dl [0.05–154.8], $P > 0.05$), while the Lp(a) levels in both groups were significantly higher than those in normotensive individuals ($P < 0.05$ and $P < 0.01$, respectively). Lp(a) was not correlated with any of the variables assessed.

The results have shown an elevated Lp(a) concentration in hypertensive NIDDM patients. Although silent coronaropathy could be present in a number of our patients in whom CHD was not diagnosed, the presence of increased Lp(a) levels in hypertensive NIDDM patients without complaints of angina or history of MI argues for an association of high levels of Lp(a) with HT in NIDDM patients, independent of CHD. Our findings confirm those of Heller et al. (6), who also obtained increased Lp(a) concentration measurements in hypertensive diabetic patients. Although they did not reach statistical significance, a very important difference of their study is that it diagnosed HT when BP levels were >160/95 mmHg. Because most of our patients were treated with antihypertensive drugs at the time of evaluation, one might speculate whether the increase in Lp(a) concentration is related to HT or to the medication.

Most of the studies that looked at the relation of Lp(a) to CHD in diabetic patients did not assess whether HT influenced the Lp(a) levels in the patients studied (1,2). Because HT is frequently associated with CHD and we have obtained significant differences in Lp(a) concentrations in normotensive and hypertensive NIDDM patients, a reasonable hypothesis would be that one cause for

the differences occurring in the literature may be the different prevalences of HT in the tested groups of diabetic patients with or without CHD. A larger-scale study to confirm these results is needed.

NICOLAE HANCU, MD, PHD
MIHAI G. NETEA, MD
SILVIA IANCU, MD

From the Diabetes Center and Clinic, University of Medicine and Pharmacy, Cluj-Napoca, Romania.

Address correspondence to Nicolae Hancu, MD, Diabetes Center and Clinic, Str. Clinicilor nr.2, 3400 Cluj-Napoca, Romania.

References

1. Velho G, Erlich D, Turpin E, Neel D, Cohen D, Froguel P, Passa P: Lipoprotein(a) in diabetic patients and normoglycemic relatives in familial NIDDM. *Diabetes Care* 16:742–747, 1993
2. Maser RE, Usher D, Becker DJ, Drash AL, Kuller LH, Orchard TJ: Lipoprotein(a) concentration shows little relationship to IDDM complications in the Pittsburgh epidemiology of diabetes complications study cohort. *Diabetes Care* 16:755–758, 1993
3. Haffner SM, Klein BEK, Moss SE, Klein R: Lack of association between Lp(a) concentrations and coronary heart disease mortality in diabetes: the Wisconsin Epidemiologic Survey of Diabetic Retinopathy. *Metabolism* 41:194–197, 1992
4. Hypertension in Diabetes Study (HDS). I. Prevalence of hypertension in newly presenting type 2 diabetic patients and the association with risk factors for cardiovascular and diabetic complications. *J Hypertens* 11:309–317, 1993
5. The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). *Arch Intern Med* 153:154–183, 1993
6. Heller FR, Jamart J, Honore P, Derue G, Novik V, Galanti L, Parfonry A, Hondekijn J-C, Buysschaert M: Serum lipoprotein(a) in patients with diabetes mellitus. *Diabetes Care* 16:819–823, 1993

Unpleasant Alcohol Effect in Diabetes Associated With 3243 bp Mitochondrial tRNA$^{Leu(UUR)}$ Mutation

Diabetes due to 3243 base pair (bp) mitochondrial tRNA$^{Leu(UUR)}$ mutation (DM-Mt3243) is a new disease entity, and its characteristic was known to be maternal transmission and an associated sensorineural hearing loss (1).

Recently, we found the clinical trait of alcohol intolerance in this subtype. Of 16 unrelated patients, 14 patients easily flush after ingestion of a tiny quantity of wine or Japanese sake (Table 1). Most of them had noticed weakness since their first experience of alcohol intake. Of 15 patients who gave consent to receive a chlorpropamide alcohol flushing (CPAF) test, all showed positive rise of facial temperature after sherry (2).

Interestingly, cases without intolerance had strange histories. One male (case 13) noticed abrupt onset of paresthesia of his left arm and chest pain. The symptoms worsened when he abused alcohol. Soon after, he developed tinnitus, hearing loss, and extreme hyperglycemia (fasting plasma glucose level 9.8 mmol/l). After he stopped abusing alcohol, all symptoms disappeared. In another case (case 11), a woman's paresthesia of legs worsened when she drank a large amount of alcohol, so she stopped drinking. Thus, all our DM-Mt3243 patients are now abstaining from alcohol consumption by their own will, irrespective of their initial alcohol tolerance.

Table 1—*Clinical characteristics, alcohol intolerance, and positivity of CPAF test of the diabetic subjects with mitochondrial tRNA$^{Leu(UUR)}$ mutation at position 3243*

Case no.	Sex	Type of diabetes	Age	Hearing impairment on audiometry	Alcohol intolerance	CPAF test	Alcohol habit at present
1	M	NIDDM	60	−	+	+	none
2	F	NIDDM	61	+	+	+	rare
3	M	NIDDM	43	+	+	+	none
4	M	NIDDM	72	+	+	+	none
5	M	NIDDM	51	+	+	+	none
6	M	NIDDM	51	+	+	+	none
7	F	NIDDM	54	−	+	+	none
8	F	NIDDM	68	+	+	+	none
9	F	IDDM	34	+	+	+	none
10	F	NIDDM	48	+	+	+	rare
11	F	NIDDM	60	+	−	+	abstinent
12	F	NIDDM	82	+	+	ND	none
13	M	NIDDM	40	+	−	+	abstinent
14	M	IDDM	37	+	+	+	none
15	M	NIDDM	68	−	+	+	none
16	M	NIDDM	60	+	+	+	none

For the CPAF test, the subjects were on 250 mg chlorpropamide daily for 3 days. After subjects drank sherry of 20–40 ml, facial warmth, facial flushing, burning of the face, and peak increment in facial skin temperature over 1°C were regarded as criteria for a positive reaction. NIDDM, non-insulin-dependent diabetes mellitus; IDDM, insulin-dependent diabetes mellitus. ND, not done; the patient did not give informed consent to receive the test. She was afraid to receive the test because she was so intolerant to alcohol.