

Modify Cardiovascular Risk Factors to Decrease Incidence of Neuropathy

Triglyceride levels, BMI, smoking patterns and hypertension appeared to affect the progression of diabetic neuropathy in this population.

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The only current treatment for diabetic neuropathy is tight glycemic control. Investigators from the European Diabetes (EURODIAB) Prospective Complications Study, however, have suggested that modifying cardiovascular risk factors in type 1 diabetic patients may lower the incidence of diabetic neuropathy.¹

Reporting in *The New England Journal of Medicine*, Solomon Tesfaye, MD, and colleagues examined the risk factors of distal symmetric neuropathy in 1,172 patients who were non-neuropathic at baseline, mean age 32.7 ± 10.2 years and diabetes duration 14.7 ± 9.3 years. Investigators hoped to signal potential modifiable risk factors for neuropathy, as morbidity and mortality rates are high among diabetic patients with neuropathy, they noted.

STRONG CONTRIBUTOR

Between 1989 and 1991, patients were randomly selected from 31 EURODIAB participating centers and assessed for total and LDL cholesterol, fasting triglycerides, body mass index, HbA1c and urinary albumin excretion rate during baseline clinical evaluations and quantitative sensory and autonomic-function testing. At mean follow-up (7.3 years), the cumulative instance of neuropathy was 23.5%, which, investigators wrote, “confirm[ed] the previously reported strong contributions of glycemic control and duration of diabetes to the risk of neuropathy.”

Neuropathy developed in patients who were older (average 3.8 years older) and had a longer duration of diabetes (average 3.3 years longer), investigators noted. Patients with hypertension, cardiovascular disease (CVD) or who smoked at baseline also developed neuropathy

There is an association between cardiovascular risk factors and neuropathy, investigators concluded.

more frequently. Furthermore, patients with micro- or macroalbuminuria or retinopathy were at an increased risk for neuropathy.

After adjusting for diabetes duration and HbA1c, investigators concluded that an association existed between cardiovascular risk factors and incidence of neuropathy. When patients were hypertensive, had elevated triglyceride levels, smoked or were obese, neuropathy developed. If patients had CVD at baseline, their risk of neuropathy was doubled (Table 1).

Hypertension had the strongest relation to the incidence of neuropathy in type 1 diabetic patients (odds ratio 1.57), as determined with a multivariate logistic-regression model that adjusted for neuropathy risk factors. The relationship, however, lost statistical significance when the definition for neuropathy excluded autonomic symptoms and autonomic-function test results. “This is consistent with our previous report that systolic blood pressure was a risk factor for the development of cardiac autonomic neuropathy,” Dr. Tesfaye and colleagues wrote.

FURTHER STUDIES

There is a need for clinical trials to confirm that modifying cardiovascular risk factors is an effective treatment for diabetic neuropathy. Such a trial should assess the use

TABLE 1. RISK FACTORS FOR NEUROPATHY AFTER ADJUSTMENT FOR HBA1C VALUES AND DURATION OF DIABETES*

Variable	Odds Ratio (95% CI)	P Value
Total cholesterol (mmol/L)	1.26 (1.10-1.45)	.001
Low-density lipoprotein cholesterol (mmol/L)	1.22 (1.03-1.45)	.02
Triglycerides (mmol/L)	1.35 (1.16-1.57)	<.001
von Willebrand factor (U/mL) [†]	1.20 (1.02-1.42)	.03
Weight (kg)	1.34 (1.17-1.54)	<.001
Body mass index	1.40 (1.22-1.61)	<.001
Waist-to-hip ratio	1.06 (0.93-1.22)	.4
Estimated glucose disposal rate (mg/kg/min)	1.37 (1.08-1.73)	.01
Albumin excretion rate (µg/min) [†]	1.25 (1.10-1.43)	.001
Insulin dose per kg of body weight (IU)	1.09 (0.95-1.26)	.2
History of smoking	1.55 (1.17-2.04)	<.001
Hypertension	1.92 (1.30-2.82)	<.001
Macroalbuminuria	2.08 (1.11-3.90)	.02
Micro- or macroalbuminuria	1.48 (1.07-2.04)	.02
Proliferative retinopathy	1.54 (0.79-2.98)	.2
Any retinopathy	1.70 (1.19-2.43)	.003
Cardiovascular disease	2.74 (1.68-4.49)	<.001

* Standardized odds ratios are expressed per SD increase in each continuous risk factor. Odds ratios for dichotomous variables have as a reference group those patients without the respective risk factor. To convert values for cholesterol to mg/dL, divide by 0.02586. To convert values for triglycerides to mg/dL, divide by 0.01129.

[†] Log transformation was used.

of antihypertensive agents in reducing cardiovascular, and in return, neuropathy risk, they suggested.

PROPER DIAGNOSIS, TREATMENT

In a related editorial, Bruce A. Perkins, MD, MPH, and Vera Bril, MD,² proposed that a clinical trial of neuropathy for type 1 diabetic patients incorporate modification of cardiovascular risks. "The focus on glycemic control should not obscure the attention owed to modifications of vascular risk factors in clinical trials in patients with type 1 diabetes," they wrote. Glycemic control, smoking cessation, blood-pressure control and dyslipidemia may be possible interventions against progression to diabetic neuropathy. Drs. Perkins and Bril are from the University of Toronto.

Of the three aspects of diabetic microvascular complications – diabetic neuropathy, diabetic retinopathy and diabetic nephropathy – neuropathy lacks proper diagnosis, prevention and treatment. "We need an indicator of early nerve damage before the development of

diabetic neuropathy, akin to early retinal changes as an indicator of risk for retinopathy or microalbuminuria as an indicator of risk for nephropathy," they wrote. ■

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1. Tesfaye S, Chaturvedi N, Eaton SEM, et al. Vascular Risk Factors and Diabetic Neuropathy. *N Eng J Med.* 2005;352:341-350.
2. Perkins BA, Bril V. Early Vascular Risk Factor Modification in Type 1 Diabetes. *N Eng J Med.* 2005;352:408-409.