Combat Diabetic Macular Edema on Several Fronts

BY BRUCE K. DIXON
Chicago Bureau

Patients with type 1 diabetes may be better protected from diabetic macular edema by improved control of glycemia, LDL cholesterol levels, and blood pressure, according to a 15-year follow-up study.

The prospective study was launched in 1990 with a cohort of 112 consecutive type 1 diabetes patients who did not have diabetic retinopathy or nephropathy at the time, according to Dr. Pedro Romero and colleagues at the Hospital Universitario Sant Joan de Reus, Universidad Rovira y Virgili, Spain.

"Our objective was to determine the epidemiological risk factors that influence the development of diabetic macular edema, in particular renal diabetic lesion (microalbuminuria or overt nephropathy)," the authors wrote in the Journal of Diabetes and Its Complications.

The half-male, half-female cohort had a mean age of 40 years and a mean diabetes duration of 23.4 years. Arterial hypertension was present in 39% of the patients.

Diabetic retinopathy was evaluated by photographs, through dilated pupils, of two 50-degree fields of each eye centered. The results were then classified as mild nonproliferative, moderate proliferative, severe proliferative, and proliferative (J. Diabetes Complications 2007;21:172-80).

Macular edema was considered present when retinal thickening involved or was within 500 mcm of the center of the macula; when hard exudates were at or within 500 mcm of the macula, if it was associated with a thickening of the adjacent retina (but no hard exudates remained after retinal thickening disappeared); and when the zone(s) of retinal thickening was (were) one disc area (or larger) in size, any part of which was within one disc diameter of the center of the macula.

The clinical classification used was the International Clinical Diabetic Retinopathy Disease Severity Scale, the investigators wrote.

After 15 years, one-half of the cohort had diabetic retinopathy (DR) and one-fifth of the cohort had diabetic macular edema (DME). More than half of those with DME had the focal type, a third were the diffuse form, and two patients had diffuse associated form to cystoid form (which is associated with diffuse form).

The mean visual acuity in patients with DME after 15 years was 0.31 in the Snellen chart test and 1.26 in the LogMAR test. The mean macular thickness was 356.21.

Factors found to be significant to the development of DME included:

▶ High levels of glycated hemoglobin. Glycemic control was classified into two groups: hemoglobin A_{1c} greater than 7.5% or less than 7.5% in concordance with the European Diabetes Policy Group. The value included in statistical analyses was the mean of all values obtained over the trial period.

▶ High levels of LDL cholesterol as defined by the American Diabetes Association categories (3.35 mmol/L or higher). In contrast to previous published research, no lipid parameters were associated with the progression of diabetic retinopathy or with proliferative diabetic retinopathy after adjustment for glycated hemoglobin and other risk factors, the investigators explained.

▶ The presence of macroangiopathy. For this, one or more of the following had to be present: symptoms of angina pectoris, history of myocardial infarction, coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, symptoms of or operation for intermittent claudication, history of amputation, transient ischemic attack, and stroke.

The authors maintained that this relationship between macroangiopathy and DME "may be explained, in part, by the increased incidence of macular edema with increased levels of lipids, which was strongly associated with the development of macroangiopathic lesions in" previous studies (Br. J. Ophthalmol. 2002;86:84-90; Ophthalmology 2002;109:1225-34).

▶ The presence of arterial hypertension, defined as a systolic measurement of 140 mm Hg or higher and a diastolic measurement of 90 mm Hg or higher.

This result contradicted an earlier finding from a 10-year study showing that the level of diastolic blood pressure was not a predictor in type 1 diabetes patients (Arch. Ophthalmol. 1995;113:601-6).

"However, a precedent study of that same group, at four years, found a positive relationship between diastolic blood pressure and the incidence of macular edema," wrote Dr. Romero and his colleagues.

▶ The severity of diabetic retinopathy, a finding which confirms previous studies.

The researchers expressed surprise that the study found no association with cigarette smoking, although an earlier study also failed to link cigarette smoking with DME (Ophthalmology 1996;103:1438-42). The current investigators hypothesize that cigarette smoking, through its deleterious effects on the retinal vasculature, may affect diabetic maculopathy.

"We did not demonstrate this effect, but if we had studied the angiographic findings in patients with diabetic macular edema, we may not have associated cigarette smoking with an increase in the development of areas of macular ischemia," they said.

"Our data suggest that better control of glycemia, LDL cholesterol levels, and blood pressure in type 1 diabetes patients may be beneficial in reducing the incidence of diabetic macular edema," the researchers concluded, adding that their results validate the current guidelines for ophthalmologic care for the detection of diabetic macular edema over the long-term course of diabetes. ■

Telmisartan's Antiproteinuric Effects Beat Those of Losartan

BY PATRICE WENDLING
Chicago Bureau

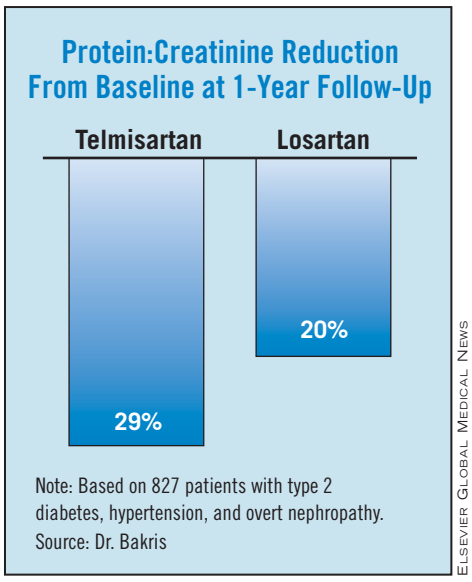
CHICAGO — Telmisartan provides greater reduction in proteinuria than losartan does after 1 year of treatment in patients with hypertension and diabetic nephropathy, Dr. George Bakris said at the annual meeting of the American Society of Hypertension.

This difference can't be attributed to differences in blood pressure control, because blood pressure reductions were comparable in patients taking either angiotension II receptor blocker (ARB), Dr. Bakris, lead investigator of the AMADEO study, said during a press briefing.

After stopping the drugs for 2 months, as per protocol, about twice as many patients on telmisartan were reported to have experienced a slightly greater antiproteinuric effect, compared with those on losartan. This is important to both the Food and Drug Administration and clinicians, because it suggests that telmisartan has done something independent of controlling blood pressure to change the natural history or biology of the disease, said Dr. Bakris.

"The differences between these ARBs in terms of receptor binding, lipophilicity, and duration of action may be responsible for the differences in the effects that you see," said Dr. Bakris, professor of medicine and director of the hypertension unit at the University of Chicago. "These data suggest that at similar levels of blood pressure control, the longer-acting, higher-binding telmisartan may confer relatively greater protection against the development of ESRD [end-stage renal disease], though that hypothesis must be tested prospectively."

Dr. Bakris and associates randomized 860 patients with type 2 diabetes mellitus, hypertension (defined as blood pressure greater than 130/80 mm Hg), and overt nephropathy to either telmisartan 40 mg or losartan 50 mg for 2 weeks, and then titrated to 80 mg and 100 mg, respectively. If blood pressure was not controlled, concomitant antihypertensives were allowed, except ARBs, angiotensin-converting enzyme inhibitors, and direct vasodilators.



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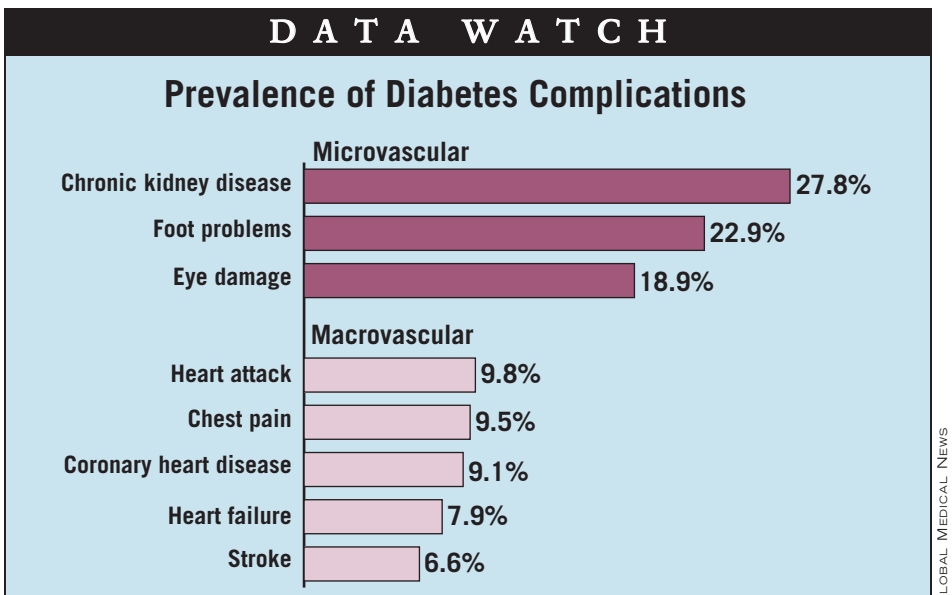
At admission, the average systolic/diastolic blood pressure was 143/80 mm Hg in both groups; mean urinary protein:creatinine ratio was 1,971 mg/gCr in the telmisartan group vs. 2,010.5 mg/gCr in the losartan group; and the mean serum creatinine was 1.54 mg/dL in the telmisartan group vs. 1.55 mg/dL in the losartan group. In all, 827 patients were available for analysis.

After 1 year of treatment, the mean change in morning spot urinary protein:creatinine—the study's primary end point—was 0.71 for telmisartan and 0.80 for losartan. This translated to a 29% reduction from baseline for telmisartan and a 20% reduction for losartan. Systolic and diastolic BP reductions were not significant between groups (–4.8/–3.2 mm Hg vs. –2.7/–2.9 mm Hg, respectively).

Among secondary end points, telmisartan produced superior reductions in urinary albumin:creatinine and prolonged the time to first cardiovascular event. There were no significant differences between the drugs in urinary sodium:creatinine, glomerular filtration rate, serum aldosterone, or high-sensitivity C-reactive protein. Adverse events were not different between groups.

Dr. Bakris disclosed that he is a consultant and speaker for Boehringer Ingelheim, which sponsored the study, and he has received research support from the firm. ■

DATA WATCH



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