Fenofibrate Cuts Retinopathy in Diabetic Patients

Those who were treated with the drug also had less progression of albuminuria and fewer amputations.

BY MITCHEL L. ZOLER
Philadelphia Bureau

ORLANDO — Treatment with fenofibrate also cut the need in the need for laser treatments for retinopathy in a controlled trial of nearly 10,000 patients with type 2 diabetes. Physicians should “consider using fenofibrate on all patients with diabetes, even patients already on a statin and at their target lipid levels, to further reduce their risk and microvascular complications,” Dr. Anthony C. Keech said at an industry-sponsored press briefing during the annual scientific sessions of the American Heart Association.

“The drug is very well tolerated and has a good safety profile,” Dr. Keech said.

Dr. Keech and his associates reported.

The results were released by the Lancet in the study of diabetic nephropathy, because these drugs reduce albuminuria, and fewer amputations, Dr. Keech said.

The benefits of fenofibrate for microvascular disease of diabetes appeared to extend beyond its significant effect on cardiovascular disease of diabetes. The results were very clear-cut. It’s exciting to use it to treat patients, and it opens a whole new area of research,” commented Dr. Virgil Brown, who is professor of internal medicine at Emory University, Atlanta.

The mean urinary albumin excretion rate fell by 71% from baseline with 40 mg/day dose of lisinopril, 56 type 1 diabetes patients with diabetic nephropathy, 40

40 mg of Lisinopril Daily Is Ideal for Diabetic Nephropathy

BY MIRIAM E. TUCKER
Senior Writer

AMSTERDAM — In type 1 diabetic patients with diabetic nephropathy, 40 mg/day of lisinopril appears to be the ideal dose for renoprotection, Dr. Katrine J. Schjoedt said in a poster presentation at the annual meeting of the European Association for the Study of Diabetes.

Angiotensin converting enzyme inhibitors such as lisinopril are considered first-line agents for renoprotection in patients with type 1 diabetes who have nephropathy, because these drugs reduce albuminuria in addition to lowering blood pressure. The currently recommended 20 mg/day dose of lisinopril is based on the drug’s blood pressure-lowering effect; the optimal dose for renoprotection has not been established, said Dr. Schjoedt of the Odense Diabetes Center, Odense, Denmark.

To evaluate whether additional renoprotective effects could be obtained with higher doses of lisinopril, 36 type 1 diabetic patients with diabetic nephropathy were taken off all ongoing antihypertensive therapy and put on fixed doses (median 60 mg/day) of slow-release formulation in the same study. After a 2-month washout period, the patients were randomized to receive 20, 40, or 60 mg/day of lisinopril for 2 months.

The 49 patients who completed the trial had a mean age of 49 years and a diabetes duration of 33 years; two-thirds of them were men. At baseline, the study patients had a mean blood pressure of 142/74 mm Hg, a mean urinary albumin excretion rate of 362 mg/24 hours, and a mean estimated glomerular filtration rate of 75 mL/min per 1.73 m².

The mean urinary albumin excretion rate fell by 71% from baseline with 40 mg lisinopril, by 70% with 60 mg, and by 63% with 20 mg. All of the reductions from baseline were significant. The 40-mg group and the 60-mg group both had significant reductions in urinary albumin excretion rate, compared with the 20-mg group, but the difference between the 60-mg and 40-mg groups was not significant.

High doses of lisinopril offer additional renoprotection. Ultrahigh doses do not offer any additional benefit.

DR. SCHJOEDT

Also, they said the criteria used to perform laser therapy were not defined in the study protocol, and therefore they probably varied among the study centers. The number of patients in the retinal sub-study was small, making it impossible to draw definitive conclusions based on 5 years of follow-up. Finally, there is no clear explanation of how fenofibrate affects diabetic retinopathy.

Possible mechanisms include documented anti-inflammatory effects of fenofibrate, the drug’s inhibitory effect on endothelial cell migration, and the drug’s reduction of apoptosis in retinal endothelial cells, said Jean-Charles Fruchtat, Ph.D., head of the department of atherosclerosis at the University of Lille, France, during the press briefing. The retinopathy effect did not appear to be mediated by an effect on blood pressure or glycemic control, because fenofibrate had little or no effect on these.

Additional evidence of beneficial effects of fenofibrate on microvascular disease in patients with diabetes comes from observations of the drug’s effect on renal function and neuropathy. Progression of albuminuria occurred in 11% of placebo patients and 9% of those on fenofibrate, a 15% relative reduction, Dr. Keech said. And regression of albuminuria occurred in 9% of patients treated with fenofibrate and 8% of placebo patients, a 14% relative increase.

In addition, amputations were lowered from a 1.5% rate with placebo to a 0.9% rate with fenofibrate, a relative risk reduction of 38% that was statistically significant. The amputation rate was reported by Dr. Keech and his associates in a separate report during the American Heart Association’s meeting.