Decreased Albuminuria by Pravastatin in Hyperlipidemic Diabetics

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Sir,

Slightly increased urinary albumin excretion (microalbuminuria) predicts the development of clinical nephropathy in type 1 (insulin-dependent) [1] and type 2 (non-insulin-dependent) [2] diabetes mellitus, and efforts have been made to reduce urinary albumin to inhibit the progression of nephropathy. Microalbuminuria is now known to be influenced by glycemic conditions [3], systemic blood pressure [4] and intraglomerular hemodynamics [5]. Recently evidences have been accumulated to show that hyperlipidemia has an adverse effect on glomerular functions in experimental animals [6]. Furthermore, reduction of proteinuria has been reported in the hyperlipidemic patients with primary glomerulonephritis treated with an HMG-CoA reductase inhibitor, simvastatin [7]. Thus, diabetic nephropathy may be affected by lipid abnormalities which often associate with microalbuminuria [8]. We report a preliminary observation about the effect of pravastatin, an HMG-CoA reductase inhibitor, on serum lipoproteins and urinary albumin in type 2 diabetic patients.

In the 12 patients (3 men and 9 women), 6 were treated with sulfonylurea and others with diet only. Mean age was 60 (range 45–78 years). They were initially administered 10 mg pravastatin per day, and the dose was increased to 20 mg per day only in the 3 patients whose serum total cholesterol levels were still higher than 220 mg/dl after 1 month. Before and after 3 months of pravastatin treatment, we measured the parameters of lipid and glucose metabolism, blood pressure, renal functions including urinary albumin/creatinine ratio in morning spot urine specimens.

Table 1. Data on lipoprotein, glucose metabolism, blood pressure and renal function before and after 3 months of pravastatin treatment

Table 1 gives the results. After 3 months of treatment with pravastatin, there was a significant reduction of cholesterol in serum and VLDL, IDL and LDL fractions, whereas triglyceride and HDL cholesterol did not change. Lipoprotein (a) also remained high. Blood urea nitrogen and serum creatinine were not changed. However, the urinary albumin/creatinine ratio was signifi-

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665

mg/g 200-
p < 0.005-
150-
100
50-

1

After
Before

Fig. 1. Changes in the urinary albumin/creatinine ratio during pravastatin treatment. The ratio significantly decreased (from 49 ± 14 to 20 ± 9 mg/g, mean $\pm$ SE, $p < 0.005$) as shown in figure 1. Glycemic conditions and blood pressure were stable during the study period.

In this study, lowering serum lipids with pravastatin was associated with the reduction in albuminuria in diabetic patients without changing glycemic condition or blood pressure. Thus, hyperlipidemia appears to be another factor affecting glomerular functions in diabetic patients with early-stage nephropathy. Glomerular cells have lipoprotein receptors [9], and hyperlipidemia may alter their cellular functions. A glomerular charge barrier may be disturbed by the deposition of apolipoprotein B. It is not ruled out that the drug has an effect on intraglomerular hemodynamics. Further studies are required to assess the mechanism of the anti-proteinuric action of pravastatin.

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