Effect of Oral Adsorbent on the Progression of Diabetic Nephropathy

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Dear Sir,

It has been reported that the administration of an oral adsorbent delays the progression of chronic renal failure in man [1]. Although its mechanism is unclear, we have recently reported that the administration of an oral adsorbent delays the occurrence of glomerular sclerosis by delaying the appearance of glomerular hypertrophy, systemic hypertension and proteinuria in nephrectomized rats [2]. Since it is postulated that all kidney diseases progress through the same nonimmunological mechanisms [3], it is suggested that oral adsorbents have a protective effect on the progression of diabetic nephropathy as well as nondiabetic renal failure. However, it is not clear when an oral adsorbent should be prescribed in diabetic nephropathy. We therefore examined whether the administration of an oral adsorbent at an early stage had an effect on diabetic nephropathy.

36 male Sprague-Dawley rats weighing 120-135 g were made diabetic, following a 24-hour fast, by intravenous injection of

65 mg streptozotocin/kg body weight (BW) and intraperitoneal injection of 0.6 ml/100 g BW of 30% glucose in 0.9% saline solution. Induction of the diabetic state was confirmed by the development of a persistent and heavy glycosuria and a blood glucose (BG) level in excess of 400 mg/dl. 24 rats demonstrating the diabetic state were on ad libitum water and standard rat chow (CE-2, Clea Japan Inc., Tokyo). After 4 weeks, the rats underwent uninephrectomy by resection. Two weeks later, the rats were divided

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Fig. 1. Change in 24-hour creatinine clearance (Ccr). □ = Control group; ■ = AST group. * $p < 0.05$; ** $p < 0.01$.

Fig. 2. Changes in urinary protein excretion (U-P) and urinary albumin excretion (U-Alb). □ = Control group; ■ = AST group. * $p < 0.05$; ** $p < 0.01$.

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Fig. 3. Histological findings. $\times 100$. a Control group, b AST group.

into 2 groups by matching the levels of BG, BW and the amount of urinary protein excretion (U-P), and the study was initiated with pair-feeding. A control group was fed the standard rat chow and the other was fed the standard rat chow containing 5% AST-120 (Kureha Chemical Industry Co. Ltd., Tokyo). Dietary intake in the control group was given by multiplying the dietary intake in the AST group by 0.95. All rats were sacrificed at week 20. BW, kidney weight, BG and systolic blood pressure at week 20 were not significantly different between the 2 groups. 24-hour creatinine clearance (Ccr), and urinary albumin excretion (U-Alb) were significantly increased from week 10 as compared to that at week 0 in both groups (fig. 1,2). The Ccr level in the AST group was significantly elevated from that in the control group at weeks 15 ($p < 0.05$) and 20 ($p < 0.05$). The levels of U-P and U-Alb in the AST group were significantly reduced from that in the control group at weeks 10 ($p < 0.05$), 15 ($p < 0.01$) and 20 ($p < 0.01$). Histological examination demonstrated that the appearance of

sclerosed glomeruli, me-sangial matrix accumulation, proteinaceous cast formation in tubules and dilatation of tubules were lower in the AST group (fig. 3). The present study indicated that AST-120 has a protective effect on the progression of diabetic nephropathy at an early stage in rats with hyperglycemia. The mechanism by which AST-120 decreased proteinuria and albuminuria is not clear. Since the administration of AST-120 improved glomerular hypertension [4], it is suggested that AST-120 decreased proteinuria and albuminuria by reducing glomerular capillary pressure. This also suggests that a vasoactive substance exists in the digestive tract of rats with diabetic nephropathy.

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