Synergetic Effect of Low Protein Diet Combined with Oral Adsorbent on the Progression of Chronic Renal Failure

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Dear Sir,

The effect of low-protein diet (LPD) on the progression of chronic renal failure (CRT) in humans is controversial. A recent multicenter trial [1] has reported the absence of benefit of LPD. In that study, the authors mentioned that the expected mean decline in the glomerular filtration rate at 3 years did not differ significantly between the usual protein diet and LPD. However, we can see the tendency for LPD to retard the progression of CRF since the decline of the glomerular filtration rate from 28 months to 36 months in LPD was low as compared to that with the usual protein diet. If that study had been continued for a longer period of time, we suggest that the effect of LPD might have become significant. On the other hand, in animals, the effect of LPD on the progression of CRF was clearly recognized from a delay in the appearance of glomerular hypertrophy, proteinuria, glomerular sclerosis and glomerular hypertension [2-4].

The administration of oral adsorbent (AST-120, Kureha Chemical Industry Co. Ltd., Tokyo) delayed the progression of CRF by inhibiting the occurrence of glomerular hypertrophy, proteinuria, glomerular sclerosis and glomerular hypertension [5, 6] similar to LPD. It has been demonstrated recently that indoxyl sulfate, an endogenous metabolite of dietary protein, promotes glomerular sclerosis and that either LPD or AST-120 reduces the level of serum indoxyl sulfate, resulting in a delay in the appearance of glomerular sclerosis [7]. There is a possibility that the mechanism by which LPD and AST-120 retard the progression of CRF is the same. Therefore we investigated whether there was a synergetic effect between LPD and AST-120.

LPD

Sixteen male SD rats weighing 285-325 g were subjected to 4/5 nephrectomy by resection. All the rats were given free access to water and LPD (14% protein). The study was started 2 weeks after surgery. One half of the animals were fed LPD and the other half were fed LPD containing...
5% AST-120. All rats were sacrificed at week 24. The results are shown in Table 1. The levels of blood urea nitrogen and serum creatinine in the LPD + AST-120 group were significantly decreased as compared to those in the LPD group (p < 0.05). Furthermore, the levels of inulin clearance and \( \gamma \)-aminohippuric acid clearance in the LPD + AST-120 group were significantly increased as compared to those in the LPD group (p < 0.05). The hematocrit tended to be higher in the LPD + AST-120 group than in the LPD group. Histological examination revealed that the index of glomerular sclerosis in the LPD + AST-120 group was significantly reduced as compared to that in the LPD group (p < 0.01). In addition, tubulointerstitial changes, such as tubular dilatation and infiltration of mononuclear cells, in the LPD + AST-120 group were milder than in the LPD group.

The present study demonstrated that LPD combined with AST-120 delayed the progression of CRF as compared to LPD alone, indicating that the mechanisms by which LPD and AST-120 retard the progression of CRF are different except for reducing the level of serum indoxyl sulfate. Since long-term treatment of LPD for CRF induced malnutrition [8] and AST-120 delayed the appearance of glomerular hypertrophy in CRF at an early stage without malnutrition [6], we recommend treatment with AST-120 from an early stage of CRF, and AST-120 treatment combined with LPD at an advanced stage of CRF.

References


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