Decrease of Urine Protein after Treatment with Probucol in Patients with Mild Glomerulonephritis and Arteriolosclerosis

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Dear Sir,

Probucol is now widely used as potent antihyperlipidemic drug [1]. Experimental studies also showed that probucol reduced proteinuria and suppressed the development of various renal injuries [2-5]. So far, however, there have been few reports showing the clinical utility of probucol in patients with nephrotic syndrome [6, 7]. In this study, we examined urine protein (UP) of 15 patients with mild glomerulopathy and hyperlipidemia who received probucol for 24 weeks. Table 1 summarizes

the characteristics of the 15 patients in addition to their serum total cholesterol (TC) and UP before and after the treatment with probucol (500 mg daily for 24 weeks). Drugs other than probucol were unchanged during the probucol treatment, and none of the patients received antihyperlipidemic drugs except probucol. The patients ranged in age from 22 to 69 years (average 45 years). 7 were male and 8 were female. Percutaneous biopsies were done in all patients, who were divided into two groups according to whether renal arteriolosclerosis was present or not. There was no significant difference in the laboratory data between the two groups before treatment. The creatinine clearance was slightly reduced (73.6 ± 22.5 mL/min totally and 67.2 ± 19.7 in the arteriolosclerotic group) but serum albumin was within normal limits (3.7 ± 0.4 mg/dl totally, and 3.6 ± 0.65 mg/dl in the arteriolosclerotic group). UP and TC are shown in table 1. 24 weeks later, the mean level of TC significantly decreased in both groups (the Student t test was used to evaluate the statistical significance). The UP also decreased significantly in patients with renal arteriolosclerosis, but not in those without it. Temporal changes in the other laboratory data including creatinine clearance were not significant [data not shown].

The current data seem to indicate the possible contribution of probucol to the decrease of UP in patients with mild glomerulonephritis with arteriolosclerosis. We could not rule out the possibility that the UP decreased spontaneously or as a result of the effects of other drugs combined with probucol. However, decrease in UP after treatment with probucol was also shown in experimentally induced nephrotic syndrome [4]. In addition, probucol showed suppressive

effects against progression in various experimental models of renal diseases [2-5]. The mechanism for such beneficial effects of probucol remains undetermined. Probucol is known to inhibit the production of oxidative LDL [8] which accelerates mesangial sclerosis [9]. A similar effect of probucol may have worked in our patients, but the current results showed that the decrease of UP was not significant in cases without renal arteriolo-sclerosis. Although renal arteriosclerosis alone seldom causes massive proteinuria, it is well known that abnormal intrarenal hemodynamics deteriorate glomerular injuries [10]. Recently, several reports have suggested that probucol suppresses the early process of renal injuries from ischemia or altered renal hemodynamics [2, 3]. We think, therefore, that the decrease in proteinuria in our patients may have resulted, at least in part, from the effects of probucol on renal hemodynamics. Previous reports failed to show the proteinuria-lowering effect of probucol [6, 7]. The reason for this inconsistency is unknown, but the difference in the duration of the treatment might have affected the result. Alternatively, the result might have been associated with the fact that the proteinuria and renal dysfunction of the previous cases were more advanced than those shown in this report [6, 7]. In addition, we could not rule out the possibility that the differences of vascular injuries might have an influence on the effects of probucol as suggested in the current results. However, the details of vascular changes were not shown in the previous reports. We think, therefore, that further studies based on careful assessment of renal changes, including renal hemodynamics, are required to discuss the clinical implication of probucol in the patient with chronic renal disease and hyperlipidemia.

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Table 1. Characteristics of patients with chronic renal disease and laboratory data before and after treatment with probucol

In patients 1-7 arteriosclerosis was present, in patients 8-15 it was not. Values for patient groups 1-7 and 8-15 are given as mean $\pm$ SD. PGN = Mesangial proliferative glomerulonephritis; DP = dipyridamole; NC = nicardipine; NF = nifedipine; FGS = focal segmental sclerosis; W = warfarin; SLE = lupus nephritis; PSL = prednisolone.

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