Dear Sir,

Atherosclerosis is reported to be accelerated in patients with chronic renal failure treated by hemodialysis [1]. Risk factors for it would include impaired lipoprotein metabolism and altered blood coagulation-fibrinolysis status. Some recent studies have shown that patients with chronic renal failure have an elevated plasma level of lipoprotein Lp(a) [2, 3], a low-density-lipoprotein-like lipoprotein having an additional protein component called Apo(a) [4]. An increased Lp(a) level is regarded as an independent risk factor for atherosclerosis in the general population [4]. High homology between Apo(a) and the kingle 4 domain of plasmin-ogen [5] may account for the proposed thrombogenic and atherogenic nature of Lp(a) [6]. Theoretically, Lp(a) competitively inhibits plasmin-mediated fibrinolysis [4]. So far, however, such a predicted suppression of fibrinolysis has not been clinically demonstrated in hemodialysis patients. To address this issue, we measured Lp(a) and coagulation-fibrinolysis parameters in hemodialysis patients before and after oral administration of niceritrol, a nicotinic acid analogue, which is known to lower Lp(a) concentration in nonuremic subjects [7].

The subjects were 17 (7 male and 10 female) nondiabetic hemodialysis patients. They were all Japanese. The mean (± SE) age was 58 ± 3 years and duration of hemodialysis treatment was 90 ± 15 months, respectively. The body mass index was 21.1 ± 0.5 kg/m². They received niceritrol (Pery-cit®, Sanwa Kagaku Kenkyusho Co. Ltd., Nagoya, Japan),
750 mg/day, for 4 weeks. Lp(a) was measured by ELISA [TintElize® Lp(a), Biopool, Umeå, Sweden]. The thrombin-antithrombin (TAT) complex concentration was measured by ELISA (Enzygnost® TAT, Hoechst Japan Co. Ltd., Tokyo, Japan) as a sensitive index of blood coagulation. D-dimer, which is one of the degradation products of cross-linked fibrin, was measured by ELISA (Asserachrom® D-Di, Boehringer Mannheim Yamanouchi Co. Ltd., Tokyo, Japan) as a molecular marker for secondary fibrinolysis. Lipoproteins were assayed by ultracentrifugation as described elsewhere [8]. Blood samples were drawn after an overnight fast before starting hemodialysis.

Table 1 gives the results. Following the treatment, Lp(a) decreased by 33%. Niceritrol did not change the TAT plasma level, whereas it significantly increased D-dimer by 15%, TAT and D-dimer showed a positive correlation both at baseline and after niceritrol treatment, suggesting a dynamic balance between coagulation and secondary fibrinolysis (fig. 1). Interestingly, the slope of the regression line became greater after niceritrol treatment. The difference between the two slopes was statistically significant (t = 2.234, d.f. = 30, p < 0.05).

One of the postulated mechanisms for accelerated atherogenesis by Lp(a) is that Lp(a) could be a competitive inhibitor for plasmin as shown in vitro [4]. Previous studies failed...
to show such an influence of Lp(a) on secondary fibrinolysis in a clinical setting [9]. In the present study, the 4-week administration of niceritrol was followed by a decrease in Lp(a), an increase in D-dimer and no change in TAT levels. Importantly, Lp(a) reduction by niceritrol treatment shifted the dynamic balance between coagulation and secondary fibrinolysis. Although there is still a possibility that niceritrol directly affected the blood coagulation system, our data can be interpreted to indicate that lowering Lp(a) attenuated the Lp(a)-mediated suppression of secondary fibrinolysis. Our observations clinically support the current concept that elevated Lp(a) interferes with the coagulation-fibrinolysis system, at least in hemodialysis patients.

References

Lp(a) and Coagulation-Fibrinolysis Status in HD Patients
Nephron 1997;77:112-113