題名:Effect of nicorandil on proteinuria in well controlled hypertensive patients.

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摘要:Proteinuria is an important risk factor for cardiovascular and renal morbidity and mortality. The effect of nicorandil on proteinuria in hypertensive patients well controlled by antihypertensive agents containing a low dose of valsartan has not been studied. PATIENTS AND METHODS: A total of 136 proteinuric (300-3000 mg/day), valsartan-treated hypertensive patients with blood pressure less than 140/90 mmHg were randomized into three groups to receive placebo, isosorbide dinitrate (30 mg/day), or nicorandil (15 mg/day) for 6 months. RESULTS: The average dose of valsartan given to the patients was similar in the three groups. Creatinine clearance remained stable throughout the study in the three groups. Nicorandil, but not isosorbide dinitrate, significantly reduced proteinuria by 44% after 6 months ($P < 0.0001$). Urinary endothelin-1 levels significantly decreased after administration of nicorandil ($P = 0.002$), whereas placebo and isosorbide dinitrate had no effect. Urinary excretion of endothelin-1 was significantly correlated with improvement in urinary protein excretion in nicorandil-treated patients ($r = 0.69$, $P < 0.0001$). The urinary excretion of retinol-binding protein decreased after nicorandil administration, probably reflecting an improvement in tubular function. In contrast, the urinary excretion of immunoglobulin G did not change significantly throughout the study in the three groups. Multivariate analysis revealed that proteinuria was only significantly correlated with the use of nicorandil (model adjusted $r = 0.35$, $P < 0.0001$). CONCLUSION: The

addition of nicorandil to treatment for patients with well controlled hypertension may have an additive effect on reducing proteinuria independent of hemodynamics and nitric oxide effects, possibly through inhibiting renal endothelin-1 synthesis and improving tubular function.