Effect of Beta-Blockade on Albumin Excretion Rate in Essential Hypertension

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Dear Sir,

The excretion of small amounts of albumin, called microalbuminuria, is well known as an early feature of glomerular impairment in diabetics. It has also been observed in patients with essential hypertension [1–3], as a consequence of altered renal hemodynamics with increased glomerular capillary pressure. In diabetics, angiotensin converting enzyme inhibitors (ACEI) have proved their ability to reduce albumin excretion rate (AER), a fact attributed to an elective vasodilation of postglomerular arteries [4]. In hypertensives however, a decrease in AER has been reported after normalization of blood pressure by antihypertensive drugs with different hemodynamic effects [1]. Thus, we designed a prospective study of the effect of an 8-week β -blocker treatment on microalbuminuria in essential hypertensives.

Fourteen patients (10 men and 4 women, mean age 46.8 ± 11.3 years, range 27–65) entered the study. They had mild essential hypertension (inclusion DBP 97.5 ± 7.1 mm Hg) for 5.2 ± 4.1 years. All of them had normal renal function measured by creatinine clearance, without macroalbuminuria or hematuria on dipstick urinalysis. None was yet treated by antihypertensive drugs at inclusion. In previously treated patients, all antihypertensive drugs were progressively withdrawn, and a 2-week wash-out period was performed before testing.

All patients received a cardioselective β -blocker, bis-oprolol, which lacks β -agonist activity. The drug was taken at a dosage of 10 mg once a day, in the morning, even the day of visits, during 8 weeks as the sole therapy.

The following measurements were performed the day before and after 2 months of treatment. Patients were requested to collect 24-hour urine the day before the test, then came in the morning as outpatients to the Nephrology Department where blood and urine samples were taken after 1 h of rest in supine position. During this period, blood pressure was measured every 6 min using an automated oscillometric device (Dinamap®). The mean of the 10 blood pressure readings was used for comparisons. Creatinine was measured on blood and urine samples by an automated Jaffé method and its clearance calculated. Albumin was measured on 24-hour and 1-hour urine using immunoturbidimetry (Turbitimer, Behringwerke AG, Marburg, FRG). This method provides a sensitivity threshold of 6 mg/l with an intra-assay variation coefficient of 3% in

our hands (data not shown). Patients were defined as having microalbuminuria (MA+) when AER exceeded 30 mg/24 h (20 µg/min).

Before treatment, microalbuminuria was found in 6 out of 14 patients. No significant difference was found between MA+ and MA- patients regarding age, weight, previous duration of hypertension and pretreatment supine blood pressure (table 1). There was no other difference between the two groups in heart rate and creatinine clearance before and after treatment. There was no difference in sodium and urea excretion between groups and between treatment periods (data not shown).

Diastolic blood pressure and heart rate decreased significantly during the study in both groups. The relative changes in these parameters were not different between groups.

Albumin excretion rate decreased significantly by 60% during treatment, but no patient returned to normal values. Both absolute and relative changes in AER were not correlated with changes in either diastolic blood pressure or creatinine clearance.

This study provides additional evidence for a large prevalence of microalbuminuria in essential hypertensives, without clear-cut differences between MA+ and MA- patients regarding the clinical features of hypertensive disease. Glomerular filtration rate was within normal range.

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Table 1. Creatinine clearance (Ccr), diastolic blood pressure (DBP) and albumin excretion rate (AER) before and after treatment in patients with (MA+) or without (MA-) microalbuminuria

	MA+	MA-
Age	39 ± 9	74 ± 12
Weight	5 ± 2	67 ± 5
Duration		
HR		
DBP		
Ccr		
AER		
years		
kg		
years		
beat/min		
mm Hg		
ml/min		
µg/min		
Before treatment		

102.2 ± 5.4
 123.5 ± 29.3
 173 ± 118
 MA- 53 ± 9
 73 ± 10
 6 ± 5
 73 ± 12
 94.0 ± 6.3
 106.3 ± 31.5
 0
 After treatment

MA +
 -
 -
 56 ± 3*
 74.7 ± 6.4*
 125.0 ± 29.3
 72 ± 35*
 MA-
 -
 -
 55 ± 8*
 77.8 ± 5.0*
 108.0 ± 44.9
 0

*p < 0.01, pre-versus posttreatment
 values, Wilcoxon
 signed rank test.

mal limits in all patients. The slight difference in GFR between MA + and MA- patients may reflect glomerular hyperfiltration in MA + , but has to be interpreted with respect to the age difference. Moreover, the lack of GFR changes during treatment argues against an important initial hyperfiltration. There was however a decrease in AER, an early marker of renal impairment [5], of which clinical implications in the evaluation of end-organ damage have been demonstrated by the reports of an increased mortality rate in microalbuminuric hypertensives [6, 7].

Regarding the strong relationship between microalbuminuria and transcapillary glomerular pressure, the decrease in AER observed in treated hypertensives is due to an improvement of glomerular hemodynamics related either to a regression of structural changes following long-term blood pressure control [7], or to a short-term pharmacological effect on the equilibrium between pre- and postglomerular arteriolar resistances. This last property largely demonstrated with ACE inhibitors, even in normotensive diabetics, is attributed to a predominant efferent vasodilation.

It has been shown that several other antihypertensive drugs effectively reduce either AER [2] or the number of microalbuminurics [8] in treated hypertensives. The present results demonstrate that even a short-term treatment with β -blocker is able to reduce AER. Since β -blockers usually induce a parallel decrease in renal blood flow and glomerular filtration rate without elective postglomerular vasodilation [9], it is suggested that the decrease in transcapillary glomerular pressure is mainly dependent on systemic blood pressure normalization.

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