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Renal Handling of Albumin and Beta-2-Microglobulin in Human Hypertension

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Dear Sir,

It has long been known that in experimental and human hypertension occurs an increased vascular permeability which may be a major contributory factor, if not the cause of the development of the hypertensive vascular lesions [1]. When extreme and sufficiently sustained elevation of blood pressure (BP) occurs as in malignant hypertension (diastolic BP ⩾ 130 mm Hg) the increase in vascular permeability becomes easily apparent in the retinal vessels by fluoroangiography [2]. In this condition, proteinuria as well is frequently demonstrable by routine analysis, whereas in the benign phase of hypertension proteinuria is regularly absent. However, *Parving* et al. [3] using radioimmunological measurements, have found that patients with mild or moderate hypertension and without clinical proteinuria, nevertheless excrete more albumin in the urine than do normotensive controls. A decrease of proximal tubular protein reabsorption seemed to be ruled out in these patients on the basis of their normal daily excretion rate of β_2-microglobulin. However, *Mogensen* et al. [4] have recently (1981) found an enhanced β_2-microglobulin excretion in 7 patients with severe hypertension.

We have studied urinary excretion of albumin and β_2-microglobulin in 26 normal subjects and 48 hyperten-

Table I. Comparison of results in patients with benign primary hypertension, accelerated or malignant primary hypertension, renal vascular disease and hypertension and controls (data are reported as MEAN ± SD)

Group		n	Sex		Mean age (range)	Creatinine clearance ml/min × 1.73 m²	Albumin excretion mg/24 h	β_2-Microglobulin excretion µg/24 h
			M	F				
A	Benign primary hypertension	24	8	16	43 (22–69)	82 ± 24 (53–139)	25.51 ± 62.73 (1.40–276.45)	239.84 ± 281.52 (18.82–1234.20)
	SBP = 168.88 ± 16.33 DBP = 103.69 ± 9.36							
B	Accelerated or malignant primary hypertension	14	11	3	44 (36–56)	66 ± 16 (41–100)	69.30 ± 109.24 (1.35–336)	1054.36 ± 1603.31 (31.92–6000)
	SBP = 224.56 ± 15.20 DBP = 123.31 ± 8.45							
C	Renovascular disease and hypertension	10	4	6	43 (34–58)	78 ± 24 (27–110)	14.32 ± 12.91 (2.30–38.40)	307.06 ± 443.30 (17.63–1482.94)
	SBP = 171.41 ± 8.21 DBP = 98.49 ± 12.65							
D	Controls	26	11	15	30 (17–46)	87 ± 20 (49–124)	8.97 ± 5.99 (1.43–29.87)	85.89 ± 48.56 (2.77–191.31)

Creatinine clearance: B vs. D $p < 0.005$; albumin excretion: B vs. D $p < 0.05$; β_2-microglobulin excretion: A vs. D $p < 0.01$; B vs. D $p < 0.005$; C vs. D $p < 0.02$.

SBP = Systolic blood pressure, mean of the group; DBP = diastolic blood pressure, mean of the group.

sive patients (table I). Criteria we used for accelerated hypertension were: retinal hemorrhages and/or exudates and diastolic BP ⩾ 130 mm Hg in several measurements during a day; for malignant hypertension, the same criteria and papilledema [5, 6]. In all hypertensive patients BP measurements were taken 5 times a day, every 4 h during the waking cycle. Mean of BP values of 3 days (5th to 7th) of observation was used to calculate mean BP of each group. All patients of the first and third group were untreated. In the second group, 11 patients had taken small and discontinuous doses generally of one drug. In none of these cases treatment included diuretics. In all cases there was no detectable proteinuria, as tested by bromophenol strips (Albustix). Differences between groups were analyzed by using Student's t test for unpaired data. Results are reported in table I. In the absence of clinical proteinuria, we have found a statistically significant elevation of urinary albumin in patients with accelerated or malignant hypertension, but not in those with benign hypertension or with renovascular hypertension. The urinary excretion of β_2-microglobulin was significantly increased in all hypertensive groups. Our results are consistent with the hypothesis that sustained severe elevation of BP can cause increased transglomerular escape of albumin. Whereas the increase of β_2-microglobulin excretion may have a similar origin, two other mechanisms may play a part: (1) with accelerating hypertension, nephrosclerosis and glomerular damage regularly occur: it may be that the corresponding tubular damage impedes reabsorption of microglobulin; (2) concerning benign hypertension, if the reabsorption of β_2-microglobulin may be considered partially mediated by sodium reabsorption, the increased β_2-microglobulin excretion may reflect an increased natriuresis (Na^+, K^+-ATPase suppression? [7]). Increased β_2-microglobulin excretion rate we observed in renovascular hypertension is explainable on the basis of a tubular damage due to ischemia.

The possible increase of urinary excretion of β_2-microglobulin in hypertension, no matter of type and degree of disease, must be taken into account whenever the excretion of this protein is used as a tubular marker in conditions other than hypertension.

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