Glomerular Hyperfiltration and Albuminuria in Essential Hypertension

A.		Losito
I.		Zampi
I.		Fortunati
A.		del Favero

Servizio di Nefrologia e Clinica Medica, Policlinico, Perugia, Italia

Attilio Losito, MD, Servizio di Nefrologia e Clinica Medica, Policlinico, I-06100 Perugia (Italy)

Dear Sir,

An association between glomerular hyperperfusion and proteinuria has been established in spontaneous hypertension in rats, a disease with many characteristics similar to those seen in essential hypertension (EH) in man [1]. We have recently found that untreated EH patients, with apparently normal glomerular filtration rate (GFR), cannot increase their resting filtration capacity after an amino acid infusion, while healthy controls do, showing that the so-called 'renal functional reserve' is severely reduced or absent and normal GFR is maintained by hyperfiltration [2].

With the aim of ascertaining whether in EH albuminuria can be related to glomerular hyperfiltration secondary to a reduced renal functional reserve, we studied the effect of a 4-hour infusion of an 8.5% amino acid solution (Freamine III, Baxter) in 17 patients (mean age 41; 11 male, 6 female) with untreated mild to moderate EH and apparently normal renal function. Two types of response to amino acid infusion were observed. In one group of 9 patients, mean basal creatinine clearance was lower and postinfusion value higher; in the second, creatinine clearance, basally higher, did not change with the infusion (table I).

Patients of the two groups were comparable for age, sex, mean blood pressure (MAP), values and duration of the disease. None of the patients had albuminuria as judged by the Albustix test. When measured by a sensitive fluorimetric assay [3], mean albumin excretion was 141 $\mu\text{g}/\text{min}$ (SEM = 45) in patients without renal functional reserve and 53 $\mu\text{g}/\text{min}$ (SEM = 16.5) in the others. The difference between the two groups increased when only patients with abnormal albumin excretion were

Table I. Albumin excretion in hypertensive patients (mean:SEM values)

Patients with renal functional reserve (n = 9)	Patients without renal functional reserve (n = 8)
--	---

450	350 ~ 7%
400	300
250	200-150
< 100	

160 180 200 220

60 80 100 120 140 Creatinine clearance, ml/min

Fig. 1. Correlation between creatinine clearance and albumin excretion in patients without renal functional reserve. $r = 0.945$, $p < 0.05$.

Glomerular Hyperfiltration and Albuminuria in Essential Hypertension

85

taken into account ($> 18 \mu\text{g}/\text{min}$); in those without renal functional reserve, mean albumin excretion was $220 \mu\text{g}/\text{min}$ ($\text{SEM} = 54$) while in the others it was $75 \mu\text{g}/\text{min}$ ($\text{SEM} = 22$) ($t = 2.68$, $p < 0.05$). Moreover, a significant correlation was found between creatinine clearance and albuminuria in patients without renal functional reserve and abnormal albumin excretion (fig. 1). These results support the suggestion that in EH there is a group of patients (or a phase of the disease) with glomerular hyperfiltration, characterized by a higher basal GFR and an absent response to amino acid infusion. Furthermore, we showed that hyperfiltering patients excrete significantly more albumin than normofiltering (a 200% difference in front of a 20% higher basal GFR). This observation lends further support to the view, derived from studies on experimental animals, that in hyperfiltering states the passage of macromolecules through the capillary wall is increased [4]. By this mechanism, uncontrolled EH can cause a hemodynamically mediated glomerulopathy [5]. Therefore, testing simultaneously the renal functional reserve and albumin excretion can help in singling out hypertensive patients at risk for progressive renal damage.

References

- Feld, L.G.; Van Liew, J.B.; Galaske, R.G.; Boylan, J.W.: Selectivity of renal injury and progression in the spontaneously hypertensive rat. *Kidney int.* 72:332–343 (1977).
- Losito, A.; Fedeli, L.; Sabalich, I.; Patoia, L.; Clausi, G.; Del Favero, A.: Assessment of renal functional reserve with amino acid infusion. *G. ital. Nefrol.* 3:191–196 (1986).
- Chavers, B.M.; Simonson, J.; Michael, A.F.: A solid phase fluorescent immunoassay for the measurement of human urinary albumin. *Kidney int.* 25:576–578 (1984).
- Olson, J.L.; Hostetter, T.H.; Rennke, H.G.; Brenner, B.M.; Venkatachalam, M.A.: Altered glomerular permselectivity and progressive sclerosis following extreme ablation of renal mass. *Kidney int.* 22:112–126 (1982).
- Brenner, B.M.; Meyer, T.W.; Hostetter, T.H.: Dietary protein intake and the progressive nature of kidney disease. *New Engl. J. Med.* 307:652–659 (1982).