



The renoprotective actions of angiotensin converting enzyme inhibitors in non diabetic proteinuric nephropathies

P. Ruggenti

Negui Bergamo Laboratories. Italy.

Chronic renal disease evolves to end-stage renal disease (ESRD) through a series of events that cause progressive parenchymal damage, which appears relatively independent of the initial insult. While the mechanisms underlying this process remain ill defined, the key lesion common to renal diseases of various etiologies is the sclerosis of the glomerular tuft. When the glomerular injury involves a critical number of nephrons, the disease progresses to terminal renal failure. Of the several theories that can explain the cause of renal disease progression, the most accredited one suggests a key role of an increase in glomerular perfusion pressure in remnant nephrons after a critical portion of renal parenchyma is lost. Intracapillary hypertension may increase glomerular ultrafiltration of plasma proteins which, in turn, may have an intrinsic renal toxicity. Among mediators of renal disease progression, angiotensin II seems to play a fundamental role in sustaining glomerular hemodynamic changes and loss of permselective function. Thus, blockade of the renin-angiotensin-system is likely critical for preventing or modulating progressive renal damage in chronic nephropathies. Indeed, angiotensin-converting-enzyme (ACE) inhibitors have been consistently reported to have a specific renoprotective effect in diabetics and non-diabetic nephropathies. In particular, the Ramipril Efficacy

In Nephropathy (REIN) study found that ACE inhibitors may halve the rate of progression to ESRD and even halt GFR decline in patients with proteinuric chronic nephropathies. However, although ACE inhibitors are the best therapy available to date for animal and human proteinuric progressive nephropathies, alone they are not always sufficient to normalise urinary proteins or to fully prevent renal damage and GFR decline. Thus, either in diabetic and non-diabetic chronic nephropathies, ACE inhibitors may reduce proteinuria by 20% to 80%, depending on the dose and length of treatment. Thus, other treatments might synergize with ACE inhibitors in further limiting protein traffic and/or interfering with events by which tubular reabsorption of filtered proteins translates into interstitial inflammation and structural damage. Multi drug approach might be targeted to: 1. maximise the response to ACE inhibitors by low sodium diet, diuretics, and intensified blood pressure control. 2. amplify the antiproteinuric effect of ACE inhibitors by the concomitant use of diverse antiproteinuric compounds which may include angiotensin II receptor antagonists (All antagonists), non-dihydropyridine type calcium channel blockers (CCBs), and non-steroidal anti inflammatory drugs (NSAID). 3. target, by endothelin receptor antagonists, for example, one of the most important vasoactive and inflammatory mediators which are up-regulated by proximal tubular cells activated by protein overload. Hoperfully, as in the past multi drug treatments allowed the oncologists to induce remission even of apparently hopeless cases, in the forthcoming years a similar approach will allow nephrologists to halt disease evolution even in most rapidly progressing nephropathies.

Correspondence: P. Ruggenti, M. D.

Negri Bergamo Laboratories

Via Gavazzeni, 11

24125 Bergamo - ITALY

Phone: +39-035-319888

Fax: +39-035-319331