

an effort to stabilize or slow the decline of renal function.

Reducing Intraglomerular Hypertension and Proteinuria

Increased intraglomerular filtration pressures and glomerular hypertrophy develop as a response to loss of nephron number. This response is maladaptive as it promotes the ongoing decline of kidney function even if the inciting process has been treated or spontaneously resolved. Control of glomerular hypertension is important in slowing the progression of CKD. Moreover, elevated blood pressure increases proteinuria by increasing its flux across the glomerular capillaries. Conversely, the renoprotective effect of antihypertensive medications is gauged through the consequent reduction of proteinuria. Thus, the more effective a given treatment is in lowering protein excretion, the greater is the subsequent impact on protection from decline in GFR. This observation is the basis for the treatment guideline establishing 130/80 mmHg as a target blood pressure in proteinuric CKD patients.

Several controlled studies have shown that ACE inhibitors and ARBs are effective in slowing the progression of renal failure in patients with advanced stages of both diabetic and nondiabetic CKD, in large part through effects on efferent vasodilatation and the subsequent decline in glomerular hypertension. In the absence of an anti-proteinuric response with either agent alone, combined treatment with both ACE inhibitors and ARBs has been considered. The combination is associated with a greater reduction in proteinuria compared to either agent alone. Insofar as reduction in proteinuria is a surrogate for improved renal outcome, the combination would appear to be advantageous. However, there is a greater incidence of AKI and adverse cardiac events from such combination therapy. On balance, therefore, ACE inhibitor plus ARB therapy should be avoided. A progressive increase in serum creatinine concentration with these agents may suggest the presence of renovascular disease within the large or small arteries.

Among the calcium channel blockers, diltiazem and verapamil may exhibit superior antiproteinuric and renoprotective effects compared to the dihydropyridines. At least two different categories of response can be considered: one in which progression is strongly associated with systemic and intraglomerular hypertension and