Uptodate より・CKD の降圧薬

Background

● In patients with chronic kidney disease (CKD), higher degrees of urinary protein excretion are associated with a more rapid decline in glomerular filtration rate (GFR), regardless of the primary cause of the renal disease and the initial GFR (figure 1). Observational studies show that patients with CKD and a diastolic pressure below 90 mmHg have better preservation of glomerular filtration rate (GFR) than hypertensive patients. Lower blood pressure targets (below 130/80 mmHg) are associated with better renal outcomes in patients with proteinuric CKD (defined as urine protein excretion greater than 500 to 1000 mg/day). (See 'Importance of proteinuria and the proteinuric response' above and 'Importance of blood pressure control' above.)

● The effect of antihypertensive drugs on proteinuria varies with drug class and salt intake: When the blood pressure is controlled, renin-angiotensin system (RAS) inhibitors such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are more effective than other antihypertensive drugs in reducing proteinuria, regardless of the etiology of CKD. This preferential effect is thought to be due to a reduction in intraglomerular

pressure and perhaps other factors. The antiproteinuric effects of ACE inhibitors and ARBs appear to be similar. (See 'Renin-angiotensin system inhibitors' above.)

The non-dihydropyridine calcium channel blockers diltiazem and verapamil have significant antiproteinuric effects in patients with proteinuria. By comparison, the dihydropyridines, such as amlodipine and nifedipine, have a variable effect on proteinuria, ranging from an increase to no effect to a fall in protein excretion. (See 'Calcium channel blockers' above.)

•Mineralocorticoid receptor antagonists (spironolactone studied more often than eplerenone)further reduce protein excretion when added to an ACE inhibitor and/or ARB. (See'Mineralocorticoid receptor antagonists' above.)

•Other antihypertensive drugs have little or no effect on protein excretion. (See 'Drugs with little or no effect' above.)

•In patients with proteinuric CKD, the antiproteinuric effect of RAS inhibitors and nondihydropyridine calcium channel blockers is greatly impaired with a high salt intake, even when blood pressure control seems appropriate, and is enhanced with salt restriction. Similar findingsare seen in diabetic nephropathy. If a low-salt diet is not achieved, administration of a diureticcan also enhance the antiproteinuric effect of RAS inhibitors. (See 'Importance of salt intake'above.)

•Multiple randomized clinical trials in patients with nondiabetic CKD, some with placebo control and some with an active control, have demonstrated a benefit of antihypertensive therapy with RAS inhibitors, mostly angiotensin-converting enzyme (ACE) inhibitors, in patients with proteinuric nondiabetic CKD. It seems likely that angiotensin receptor blockers have a similar renoprotective effect as ACE inhibitors in nondiabetic CKD but supportive data are limited. Additional evidence in support of a preferential benefit with ACE inhibitors in proteinuric patients has come from metaanalyses. (See 'Effect of renin-angiotensin system inhibitors on progression of CKD' above.)

●Post-hoc analyses of these and other studies have shown correlations between the reduction in proteinuria with therapy and slower progression of renal disease. (See 'The proteinuric response as a predictor of outcome' above.)

●When trying to slow the progression of nondiabetic CKD, protein excretion above 500 to 1000 mg/day identifies patients who are most likely to benefit from antihypertensive therapy with RAS inhibitors. By contrast, there appears to be no preferential benefit of RAS inhibitors in patients excreting less than 500 mg/day. (See 'Lack of benefit in nonproteinuric CKD' above.)

●The three major trials in adults that evaluated the effect of goal blood pressure

on CKD progression suggest that the renal benefit of more aggressive blood control is primarily restricted to patients with higher rates of protein excretion (figure 2). Meta-analyses of randomized trials support this conclusion. (See 'Effect of goal blood pressure on progression of CKD' above.)