Kidney Disease Analysis-A Study

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Kidney disease is a frequent complication of diabetes, cardiovascular disease, and obesity. Advancement in biomedical research created opportunities to study kidney disease in a variety of platforms. This article discusses the kidney in hypertension, diabetes, and monogenic forms of kidney disease, as well as the cellular and molecular mediators of acute kidney injury and fibrosis, IgA nephropathy and idiopathic membranous nephropathy, and kidney transplantation. A new insights into focal segmental glomerulosclerosis and the role of podocytes in health and disease are discussed.

The medical and scientific communities viewed kidney dysfunction, although devastating to the unfortunate affected individuals, as rare and of minimal consequence to population health. With uniform definitions, it is known that kidney disease is common. The presence of chronic kidney disease (CKD) is associated with significantly more adverse outcomes for patients with cardiovascular disease and diabetes compared with individuals without CKD.

The two principle outcomes of CKD are progressive loss of renal function, and the development and progression of cardiovascular disease (CVD). Hypertension is both a cause and consequence of CKD. The prevalence of hypertension is inversely related to glomerular filtration rate (GFR). Observational and interventional studies show that BP reduction slows the rate of progression of CKD. In a meta-analysis of 84 randomized and non-randomized trials in CKD patients, for each 10 mmHg drop in mean arterial pressure (MAP) there was an improvement in rate of loss of GFR.

In respect of specific BP targets in India randomized trial was made on 1148 type 2 diabetics to BP goals of <150/85 mmHg and <180/105 mmHg. The mean achieved BPs were 144/82 mmHg and 154/87 mmHg, respectively. There were 37% fewer microvascular complications (including ESRD) in the group with the lower target. The Modification of Diet in Renal Disease (MDRD) trial randomized 840 patients with CKD 3 and 4 to a ‘usual BP’ goal (140/90 mmHg if ≤60 year, 150/95 mmHg if >60year) or a ‘low BP’ goal (125/75 mmHg and 135/80 mmHg, respectively). In all patients, there was a linear relation between increasing MAP and rate of loss of GFR, the effect being greater in patients with higher degrees of proteinuria. So it is suggested a BP target of <130/80 mmHg for patients with CKD and <125/75 mmHg for those with >1 g/day of proteinuria.

Proteinuria is common in CKD patients and is a strong independent risk factor for progression. Proteinuria reduces the risk of CKD progression. In non-diabetic CKD it is found an 80% reduction in the relative risk of CKD progression per gram/day reduction in proteinuria.

BP reduction will reduce proteinuria and a meta-analysis of 84 studies demonstrated that proteinuria reduction was proportional to BP reduction in both diabetic and non-diabetic renal disease. However, some studies are able to show an effect of proteinuria reduction on CKD progression independent of BP control. In a post hoc analysis of 273 patients with proteinuric nephropathies, patients with the greatest short-term reductions in proteinuria had the slowest declines in GFR, regardless of BP control. In a post hoc analysis of the Reduction in Endpoints in Noninsulin-Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan (RENAAL) study of type 2 diabetics, every 50% reduction in albuminuria produced a 36% risk reduction for doubling of serum creatinine and 45% for ESRD during later follow-up.

Some study again in type 2 diabetics, demonstrated the risk of ESRD doubled for each doubling of baseline proteinuria, and conversely for each halving of proteinuria over the treatment year the risk of ESRD was reduced by more than half. Proteinuria reduction should be targeted to slow CKD progression.

Specific anti-hypertensive drugs may reduce proteinuria and slow CKD progression independent of BP effects, with the most rigorous data supporting the use of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs).

In non-diabetic CKD, meta-analyses demonstrate that ACEIs and ARBs can reduce proteinuria. In diabetic CKD, meta-analyses demonstrate that ACEIs in type 1 diabetics, and both ACEIs and ARBs in type 2 diabetics, increase the probability of regression from microalbuminuria to no albuminurua. One study found that this effect was not completely abolished by adjusting for BP. ACEIs also reduce the rate of progression of microalbuminuria to macroalbuminuria in type 1 and 2 diabetics as do ARBs in type 2 diabetics. Finally, two further meta-analyses demonstrate that...
ACEIs can reduce albuminuria in diabetics.

Combination therapy with ACEIs and ARBs has also been assessed in two meta-analyses that included diabetic and non-diabetic patients with CKD 3. Combination therapy significantly reduced proteinuria independent of BP, without causing clinically relevant changes in serum potassium levels or GFR.

In terms of other agents, one meta-analysis has reviewed the effects of calcium channel blocker (CCB) subclasses on CKD progression. Non-dihydropyridine CCBs significantly reduced proteinuria independent of BP changes when compared with dihydropyridine CCBs. There are also RCTs supporting the use of the thiazide diuretic indapamide in type 2 diabetics with hypertension with a reduction in microalbuminuria comparable with that achieved with the ACEIs, enalapril and captopril. Future studies may increase the body of evidence supporting the use of these drugs in CKD.

Three meta-analyses have also demonstrated a reduction in the rate of progression of CKD with both ACEIs and ARBs. Two demonstrated that ACEIs reduced the risk of CKD progression by 30–40% but could not confirm the independence of this effect from BP control alone. In the other, including 1860 patients with non-diabetic CKD, ACEIs reduced the risk of progression of CKD by about 30% adjusting for BP and proteinuria. However, the benefit of ACEIs was unclear below a baseline urinary protein excretion of 0.5 g/day.

Three meta-analyses question the renoprotective effects of renin–angiotensin–aldosterone system (RAAS) blockade. One demonstrated a significant reduction in proteinuria in 142 patients with polycystic kidney disease (PKD) treated with ACEI, but only a trend towards slowing CKD progression. Another meta-analysis of diabetic nephropathy progression showed a trend only to risk reduction with ACEIs. However, this included a large study assessing those with a high cardiovascular risk rather than renal risk per se which may have skewed the analysis. Finally, although a recent meta-analysis of 13 RCTs including 37 089 patients with various causes of CKD demonstrated a reduced risk of progression of CKD in those on ACEIs or ARBs, no benefit was seen in the diabetic sub-population. However, the largest trial in this meta-analysis Antihypertensive and Lipid-Lowering Treatment to Prevent Heart attack Trial (ALLHAT) accounted for 33 357 of the patients studied. Not only was there a lower BP in the control group of this study which could have negated the benefits of RAAS blockade, but again, this was a cardiovascular study in patients at low risk for CKD progression.