Hypertension and Cardiovascular Risk in Chronic Kidney Disease Patients

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This supplement of the Journal of American Society of Nephrology contains some of the proceedings of the Fifth International Conference on Hypertension and the Kidney. The Conference, held in Madrid, Spain, in February 2006, was organized by the Department of Nephrology of the Hospital General, Universitario Gregorio Marañón, under the sponsorship of the Universidad Complutense de Madrid, Spanish Society of Nephrology, Spanish Society of Hypertension, and European Renal Association–European Dialysis and Transplant Association.


The Fifth International Conference on Hypertension and the Kidney this year was dedicated to renal dysfunction as a cardiovascular risk factor, from the initial vascular lesion characterized by microalbuminuria and renal dysfunction to the advanced disease defined by chronic kidney disease stages 4 and 5, and by those receiving chronic dialysis and those with elevated cardiovascular risk after transplantation. Elevation of serum creatinine and reduced creatinine clearance are strong predictors of cardiovascular death. Furthermore, it has been shown in several studies in the general population that early renal damage, manifested by microalbuminuria, also increases the relative risk of cardiovascular events. The traditional Framingham cardiovascular risk factors are elevated in patients with kidney diseases; however, this conference is focused on other, nontraditional cardiovascular risk factors that occur in chronic kidney disease such as inflammation, malnutrition, oxidative stress, and abnormal mineral metabolism, among others, which promote and accelerate atherosclerosis. The final result of these high levels of cardiovascular risk in chronic kidney disease is a condition with high cardiovascular morbidity and mortality.

In the initial phases of chronic kidney disease, there is increased production of free radicals in the form of O2, oxidative stress that induces chronic inflammation, endothelial dysfunction, and progressive vascular damage. Numerous clinical and animal studies have demonstrated that inflammation plays a prominent role in all stages of the atherothrombotic process. Inflammation is a key step in the progression and complications of atherothrombosis and elevation of various plasma or serum markers of inflammation, including acute phase reactants, cytokines, and adhesion molecules. This suggests that the inflammatory process is more systemic than local. In the last several years, various inflammatory markers have proven useful as predictors of future coronary events in both the general population and among those with previous coronary artery disease. Many of the reports in this supplement analyze the role of these inflammatory markers in the vascular risk of patients with chronic kidney disease.

Additionally, patients with chronic kidney disease have a high prevalence of insulin resistance and the metabolic syndrome, which is another proinflammatory state associated with alterations in cytokines produced in the abdominal fat, i.e., leptin and adiponectin (elevation in the case of leptin and reduction in the case of adiponectin). These cytokines exert opposite metabolic effects on the cardiovascular system. Leptin plays important roles in the development of hypertension associated with abdominal obesity and is proatherogenic, whereas adiponectin increases insulin sensitivity and has anti-inflammatory and antiatherogenic properties. Moreover, at the present time the role of these adipose tissue cytokines in renal failure patients has not been established.

The treatment of dyslipidemia, which is commonly encountered in chronic kidney disease, was another important topic in this conference. The benefit offered by statins in the prevention of vascular damage is not due solely to their effect on hypercholesterolemia; there are also antiinflammatory and possibly antiproliferative properties as well. It is interesting to emphasize the antiinflammatory role of statins in patients with chronic kidney disease. These medications are HMG-CoA reductase inhibitors and they are the most potent drugs for the reduction of plasma cholesterol levels, having shown efficacy in the prevention (primary as well as secondary) of coronary disease. The benefits of statins in the prevention of cardiovascular disease appear to be greater than expected relative to their capacity to lower cholesterol alone. It is suggested that they have other benefits beyond antilipemic effects. These beneficial effects, which are not dependent on decrease in the level of cholesterol, have been called “pleiotropic” effects. These pleiotropic effects include improvement in endothelial function, atherosclerotic plaque stability, reduction in oxidative stress and...
inflammation, and inhibition of the thrombogenic response. The antiinflammatory effects are considered key among the benefits of statin therapy in reducing cardiovascular mortality. However, there are not many studies that analyze this therapeutic aspect of statins in patients with chronic kidney disease.

Finally, abnormal mineral metabolism, especially hyperphosphatemia, is now recognized as an important and modifiable cardiovascular risk factor among dialysis patients and in earlier stages of chronic kidney disease. Recent work has highlighted a potential mechanism for the increased cardiovascular risk among hyperphosphatemic dialysis patients, i.e., left ventricular hypertrophy. *In vitro* studies have demonstrated that hyperphosphatemia can induce procalcifying phenotypic changes in vascular smooth muscles cell, which strongly suggests that cardiovascular calcification mediates adverse cardiovascular effects of abnormal mineral metabolism. Control of hyperphosphatemia in patients undergoing daily hemodialysis for three hours each session, six times per week, has been correlated with reduction in left ventricular mass at one year of follow-up. This suggests that hyperphosphatemia may have reversible effects on left ventricular mass, which is an important predictor of cardiovascular events in end-stage renal disease patients.

In summary, the reports in this supplement highlight recent advances presented at the Fifth International Conference on Hypertension and the Kidney in new arenas of novel cardiovascular risk factor research. We hope that the *JASN* readership benefits from and enjoys reading about these advances.

We are grateful to all distinguished contributors to the Conference for both in their lectures at the Conference and for their published reports. We would also like to express our gratitude for the interest shown by the Editor-in-Chief of *JASN*, Dr. William Couser, who kindly favored the publication of this special issue and also to Bonnie O’Brien, Managing Editor of *JASN*, for her editorial assistance.