AMS Archives of Medical Science

The global burden of chronic kidney diseases waits for better renoprotection

Chronic kidney disease (CKD) is a worldwide threat to public health, but the scale of the problem is probably not fully appreciated [1]. In recent decades, we have seen a shift in the major cause of death and disability from nutritional deficiency and infections diseases toward non-communicable diseases, with the highest mortality caused by cardiovascular diseases (CVD). The growing prevalence of CKD is one aspect of this shift. CKD has, indeed, a complex interrelationship with cardiovascular disease, hypertension and diabetes [2]. Of note, diabetes affected 2.8% of the global population in 2000, and this will triple to 6.8% by 2030 [3]. By this time, 81% of those with diabetes will live in the developing world, almost three times the rate of increase compared with developed countries. About 40% of patients with type 2 diabetes will develop CKD. The estimated global dialysis population for end-stage chronic kidney disease will exceed 2 millions by the year 2010, expanding at a rate of 7% per year, with an aggregate cost of more then US$ 1 trillion [4]. Much less is known about the prevalence of earlier stages of CKD, when symptoms may be mild or neglected by patients or their caring physicians. According to the third National Health and Nutritional Examination Survey (NHANES), the estimated prevalence of CKD is 11% of the adult population in the United States [5]. If these data were to be extrapolated to the world population, the number of people with CKD could be estimated as hundred of millions [6]. A sizeable proportion of these patients will eventually progress toward end-stage renal disease and will require renal replacement therapy. With the rising number of patients involved, costs for renal replacement therapy, will become extremely high and prohibitive not only for developing countries. Thus, efforts have to be made to stop progression or even induce remission/regression of renal disease to avoid end-stage renal failure.

At present, there is no specific cure for most of the acquired CKD. This implies that our effort should focus on getting more insights about mechanisms and mediators involved in renal disease progression to ultimately develop targeted renoprotective strategies. Certain renal diseases, although rare, have a rapid course that quickly leads to irreversible ESRD. More common nephropathies progress less rapidly, but still evolve to ESRD within one to four decades after diagnosis. During the past 20 years, research in animals and humans have provided significant information on the mechanisms by which CKD progress and has indicated preventive strategies [7]. Many studies have established that progressive deterioration of renal function is the result of compensatory glomerular hemodynamic changes in response to nephron loss due to various original insults. However, there is robust evidence that progression of chronic nephropathies is multifactorial.

This issue of *Archives of Medical Sciences* highlights the current knowledge on the pathophysiology of progressive CKD and discusses initially the more traditional factors and their mechanisms to injure the kidney, namely proteinuria and high blood pressure. Focus is also on more recent players such dyslipidemia, endothelial dysfunction and oxidative stress that all participate to chronic renal injury through activation of pro-inflammatory and pro-fibrotic mechanisms. Anemia is a further risk factor for progression of CKD that is examined, particularly for its implication in linking CKD and cardiovascular risk. The topic of treatment is then addressed by first examining more established therapies, such as those to modulate the renin-angiotensin-aldosterone system, that can be used for renoprotection in proteinuric nephropathies. For non-responders or partial responders, treatment procedure to remission and/or regression must include a multi-pharmacological strategy that is also covered in depth in this issue of the Journal. With the focus on renoprotection is also the discussion about the controversial role of calcium antagonists in CKD.

Chronic kidney disease encompasses different types of renal diseases and the biggest group includes glomerular disease of which diabetic and hypertensive nephropathies are the most common cause of CKD. There are also immune-mediated, inflammatory glomerular diseases. The present issue of *Archives of Medical Sciences* discusses the more recent insights about target antigens, mediators, and pathways of renal injury of two prototypic immune glomerulopathies, such as idiopathic membranous nephropathy and lupus nephritis. There is a clear need to find further therapies to better control antibody production in immune-related nephropathies. It seems likely

that biological agents that are directed at B-cell depletion or inhibition will form part of the immunotherapeutic armamentarium in the future treatment of immune-mediated glomerulopathies.

Overall, novel drugs and biologics to target the inflammatory and profibrotic processes underlying CKD are now being testing in clinical trials. As existing drugs for the treatment of chronic nephropathies have a favourable risk/benefit ratio, new therapies to induce renoprotection will require a similar or better safety profile if they are to be widely used and accepted.

Giuseppe Remuzzi MD, FRCP, Prof
Director, Negri Bergamo Laboratories and Clinical Research Center
for Rare Diseases "Aldo e Cele Dacc'o"
Director, Unit of Nephrology and Dialysis,
Ospedali Riuniti Bergamo, Bergamo, Italy

Reference

1. Dirks J, Remuzzi G, Horton S, Schieppati A, Rizvi SA. Disease Control Priorities in Developing Countries. Jamison DT, et al. (eds.). Oxford University Press and the World Bank, New York 2006.
2. Collins AJ. The haemoglobin link to adverse outcome. Adv Stud Med 2003; 3: S14-S17.
3. Wild S, Roglic G, Green A, Sicree R, King I. Global Prevalence of Diabetes. Diabetes Care 2004; 27: 1047-1053.
4. Lysaght M. Maintenance dialysis population dynamics: current trends and long term implications. J Am Soc Nephrol 2002; 13: S37-S40.
5. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: third National Health and Nutrition Examination Survey. Am J Kidney Dis 2003; 41: 1-12.
6. Remuzzi G, Weening JJ. Albuminuria as early test for vascular disease. Lancet 2005; 365: 556-557.
7. Perico N, Benigni A, Remuzzi G. Present and future drug treatments for chronic kidney diseases: evolving targets in renoprotection. Nature Rev Drug Discov 2008; 7: 936-953.