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Prevention of chronic renal disease progression

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Preventing renal disease from progressing to end-stage renal failure (ESRF) is not only a medical challenge, but also a growing social and economic problem in many countries. The identification and correction of physiological and metabolic hanges that may contribute towards progressive renal deterioration is thus crucial.

Proteinuria and hypertension are the major factors contributing to the progression of chronic renal disease and effective antihypertensive therapy is currently the single most important treatment i chronic renal insufficiency (CRI) pateints; this also in the perspective that lowering blood pressure in the major determinant of proteinuria reduction. Some hypertensive agents may be capable of reducing CRI progression not only because of their antihypertensive and antiproteinuric effects, but also because they may halt some of the pathogenetic mechanisms involved in glomerular and tubulo-interstitial renal damage. There seems to be a clear difference in the antiproteinuric capacity of the different classes of antihypertensive drugs, with ACE inhibitors, angiotensin II receptor antagonists (AT1RA) and non-dihydropyridine calcium channel blockers (CCB_S) having the greatest capacity to reduce urinary protein excretion. However, it seems that, after a significant decrease in blood pressure, the antiproteinuric effect of all of the antihypertensive drugs became nearly the same, although this should be tested in randomised, controlled trials. According to the results of large trials, ACE inhibitors also significantly reduce the rate of loss of renal function in diabetic and non-diabetic chronic renal diseases; this effect is greatest in patients with substantial proteinuria at baseline. It is worth noting that the HOPE study strongly supported the use of ACE inhibitors as preventive agents for patients at high risk of cardiovascular events (such as CRI patients). AT1RAs have recently been proved of benefit in type 2 diabetic nephropathy. The possible renoprotective effect of CCBs is still controversial. The possibility that combination treatments with some classes of antihypertensive drugs (i.e. ACE inhibitors, CCBs, AT1RAs) may have additive or even synergistic renoprotective effects other than blood presure control is extremely fascinating, also considering that multidrug antihypertensive regimens are required to obtain the present blood pressure target in the majority of patients with CRI; however, this has still to be proved.

Dyslipidemia is common in patients with chronic renal disease, especially in those with more severe CRI or the nephrotic syndrome. Since the first observation that lipids accumulate within scarred kidneys, it has been suggested that dyslipoproteinemia contributes towards the progression of glomerular and tubular lesions, which leads to a subsequent deterioration in renal function. While awaiting for the results of ongoing trials about the possible role of statins in the prevention of CRI progression, lipid-lowering therapy can not still be recommended for renoprotection. However, recommendations should also be based on the well established cardiovascular risk associated with hyperlipidaemia. In addition, statins may influence important intracellular pathways that are involved in inflammatory and fibrogenic responses leading to vascular disease. This is likely to be all the more relevant in patients with ESRF, whose cardiovascular morbidity and mortality is considerably increased.

Dietary protein restriction is effective in slowing down the rate of CRI progression, but this effect marginally delay the time when ESRF is reached. For this reason, very-low-protein intakes or vegetarian regimens should be considered only in highly motivated patients, without forgetting that the risk of malnutrition. The calcium and phosphorus metabolism seems not to play a major role in the progression of renal injury, at least in the early phase; further studies are needed to elucidate whether lipid abnormalities have a casual role in CRI progression or they are merely a consequence of metabolic derangements. However, given that hyperphosphoremia, hyperparathyroidism and dyslipidemia may contribute to the development of cardiovascular disease in CRI patients, great attention has to be paid to the treatment of these conditions.

Finally, it is important to stress that general medical care is a very strong determinant of patient outcome in the conservative phase of CRI treatment. For this reason intervention has to be tailored to each patient in order of not only preserving residual renal function, but also guaranteeing patient well-being