**Treatment of hypertension in patients with chronic renal failure**

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**Introduction**

Patients with chronic renal failure (CRF) should be classified in three categories: (i) those with renal insufficiency of various degrees, (ii) those receiving haemodialysis or peritoneal dialysis, and (iii) the renal graft recipients (RGR) in whom there is almost always some degree of renal insufficiency.

Cardiovascular disease (CVD) is the leading cause of death in CRF patients with a death rate of 3.5 times higher compared with that of a non-renal cohort with similar ages.

Hypertension, which is an important risk factor for morbidity and mortality from CVD in the general population, is an extremely common finding in CRF patients with a prevalence ranging from 60 to 100%, depending on the target population.

Although there is substantial experimental and clinical evidence that controlling blood pressure will slow the decline in renal function in patients with renal insufficiency, the reports on the relationship between blood pressure and CVD mortality in dialysis patients are conflicting.

**Slowing the rate of progression to end-stage renal disease**

Clinical studies have convincingly shown that antihypertensive treatment slows the progression of both diabetic and non-diabetic nephropathies. It is of great importance, however, that the effectiveness of therapy appears to be related to the level of blood pressure control in relation to the degree of proteinuria. According to the MDRD study aggressive blood pressure lowering is particularly important in proteinuric patients. Based on the results of the above, as well as of other studies, the JNC-VI Hypertension Treatment Guidelines 1997 recommends a target blood pressure of less than 125/75 mmHg in patients with CRF and proteinuria in excess of 1 g/24 h, and blood pressure less than 130/85 mmHg in patients with proteinuria less than 1 g/24 h.

As there are no prospective studies yet, regarding the optimal blood pressure control in kidney graft recipients, it is justifiable to suggest for them the same JNC-VI guidelines applied to chronic renal insufficiency patients.

Regarding the drugs of choice, ACE inhibitors (ACEi), which have been used in the above mentioned clinical studies, are the favourable drugs, as they have a specific renoprotective effect distinct from the level of blood pressure. Angiotensin receptor blockers (ARBs) are also promising drugs as they can reduce proteinuria to the same level as ACEi. Furthermore, in recent, but yet unpublished, long-term studies (i.e. IDNT, IRMA II, RENAAL), it has been shown that administration of ARBs significantly reduces proteinuria and delays the progression of end-stage renal disease (ESRD). However, monotherapy is often inadequate to control blood pressure and other drugs must be added to the antihypertensive treatment. A non-dihydropyridine calcium channel blocker (CCB, i.e. verapamil or diltiazem), which can also reduce proteinuria should be used as a second drug while a diuretic, mainly furosemide, is necessary in cases of impaired renal function.

**Prevention of cardiovascular disease**

Left ventricular hypertrophy (LVH), which is a marker of cardiac disease is progressively increasing as the GFR declines reaching a prevalence of 75% in dialysis patients. This prevalence of LVH is almost four times higher compared to that of the general population. Much higher is the rate of clinical heart failure in dialysis patients (40%) compared to that of the general population (5%). In RGR LVH prevalence is less than that of dialysis patients (50 vs 75%) but still high. It is, therefore, obvious that prevention of LVH is mandatory and should start very early in the process of GFR reduction. The pathogenesis of LVH in CRF patients is multifactorial with two major mechanisms: hypertension, which is responsible...
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for the concentric hypertrophy and anaemia, which causes eccentric LVH. According to these mechanisms, both hypertension and anaemia as well as other cardiovascular risk factors such as dyslipidaemia, hyperglycaemia, and hyperhomocysteinaemia should be treated in parallel.

Regarding treatment of hypertension, three questions should be answered: When should we start treatment, which level of blood pressure should be targeted and which treatment should be administered? The absence of large, randomized controlled trials makes it difficult to define optimal blood pressure target in dialysis patients.

According to the JNC-VI [11], nephropathy is considered as target organ damage and, therefore, patients with even high-normal blood pressure levels (130–139/85–89 mmHg) should start drug therapy.

Regarding the target of blood pressure there are no data or guidelines for dialysis patients. We can use, however, the results of the Hypertension Optimal Study 1997 [15], which showed that the reduction rate of cardiovascular events was higher with blood pressure levels of 138/83 mmHg. How can we achieve this target? The preferred therapy (before any or concomitant drug therapy) is the control of extracellular volume and maintenance of dry weight. The fact that better blood pressure control is due to adequate control of the extracellular volume has been shown at the Tassin Center where control of the blood pressure by the ‘dry-weight method’ markedly reduced the incidence of cardiovascular complications [16]. Anti-hypertensive agents may be necessary in addition to volume control to normalize blood pressure. There is no comparative study of anti-hypertensive drugs in dialysis patients. Drugs that are actually prescribed are: CCBs, ACEi, β-blockers and sympatholytics.

Peritoneal dialysis patients could at least theoretically be easier maintained at dry weight, which should facilitate better blood pressure control and decrease cardiovascular morbidity and mortality. However, recent studies indicate that this goal is often not achieved in practice. Treatment of hypertension in these patients also demands extracellular volume reduction.

Conclusions

Hypertension plays an important role in the development and progression of CRF in patients with primary chronic renal disease, and in RGR. There is also strong evidence suggesting that hypertension is associated with cardiovascular manifestations that lead to cardiomyopathy and cardiac failure in the above patient population. However the treatment of hypertension is mandatory in all patients with CRF and must be started as early as possible.

References