FOREWORD

This *Drugs* supplement updates the current knowledge about manidipine, a third-generation calcium channel antagonist. Calcium channel antagonists are popular antihypertensive agents because of their highly acceptable tolerability profile and their efficacy in lowering blood pressure in patients of all ethnic groups, irrespective of age. The controversy about their long-term safety, raised 10 years ago, is now over, as randomised, controlled trials have clearly shown that calcium channel antagonists have the same long-term efficacy and safety as the older drug classes. Compared with diuretics and β-blockers, calcium channel antagonists may offer greater protection against stroke and less protection against heart failure, resulting in similar overall cardiovascular benefit.

Several calcium channel antagonists are currently available in many European countries, and one may ask whether it is worth developing novel molecules. Progress in the pharmacology of calcium channel antagonists has been targeted at reducing the reactive sympathetic activation and the occurrence of ankle oedema, and at reaching a certain degree of renal selectivity. The article written by Sylvain Richard presents recent data about the expression and physiological role of calcium channels in arteries and the molecular targets of the calcium channel antagonists, particularly those exhibiting distinct renovascular effects.

In their review, Alex Roca-Cusachs and Filippos Triposkiadis give broad evidence of the antihypertensive effects of manidipine, not only in the middle-aged uncomplicated hypertensive population but also in patients at high cardiovascular risk, such as elderly patients and patients with chronic renal disease and diabetes.

The reviews in this supplement provide a clear overview of the profile of manidipine and of its two main advantages. First, by contrast with several dihydropyridines (DHPs), manidipine does not increase plasma norepinephrine. In his paper, Roberto Fogari examines the mechanisms put forward to explain the formation of ankle oedema during calcium channel antagonist therapy (including arteriolar vasodilation, impairment of local vascular autoregulation of blood flow and impaired protection against hydrostatic load), and suggests specific pharmacodynamic properties of manidipine explaining the lower incidence of ankle oedema, compared with most DHPs. The lack of sympathetic activation by manidipine can also exert a protective effect on other target organs, like the coronary and the renal circulations, the large arteries, and the cerebral vasculature. This remains to be confirmed in clinical studies.

Second, manidipine demonstrated its vasodilatory effect not only on the renal afferent arterioles, as with other DHPs, but also on the efferent arterioles, which enables it to lower blood pressure without producing any increase in intraglomerular pressure and renal damage. These advantages, which have been substantiated in clinical trials measuring albuminuria and proteinuria in diabetic hypertensive patients, are detailed by René Wenzel.

Finally, Alberto Zanchetti, in his concluding remarks, reviews the current evidence-based guidelines about blood pressure lowering and the place of manidipine among the currently available calcium channel antagonists and other classes of antihypertensive agents. Altogether, these articles indicate that manidipine not only provides an additional treatment option for patients for whom DHP calcium antagonists are appropriate, but also that its use could promote increased patient renal protection and compliance, thereby favourably influencing hypertension-related morbidity and mortality.

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