Role of the fixed-dose combination lercanidipine–enalapril in renal protection

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ABSTRACT

Even with the availability of novel and efficacious antihypertensive agents, an insufficient number of hypertensive patients achieve their desired blood pressure (BP) target. This failure is partly due to the fact that many patients do not strictly adhere to their drug therapy and/or they report the presence of adverse effects. Traditionally, monotherapy is used as first-line treatment to achieve BP targets; however, when this fails, combination therapy is then required. In light of the need to attain BP goals, combination therapy (especially fixed-dose) is currently recommended. The main advantages of combination therapy over monotherapy are not only that of reduced dose, improved efficacy and reduced adverse effects, but also of target protection and reduced cardiovascular (CV) risk. Therefore, the development of single-administration drug combinations should also improve patient adherence to therapy and therefore help in achieving BP control. Among the various combinations available, calcium channel blockers (CCBs) and angiotensin-converting enzyme (ACE) inhibitors have been proven to be extremely effective, while also displaying good tolerability. Individually, both the third-generation CCB lercanidipine and the ACE inhibitor enalapril are effective antihypertensive agents. In addition, both of these agents also show other beneficial effects when administered as monotherapy. Of particular importance is the fact that when lercanidipine plus enalapril are administered in combination, they show synergism, thus providing added efficacy with reduced side effects. The present report provides an overview of the main clinical studies examining lercanidipine and enalapril administered as monotherapy, with particular focus on the potential renoprotective effects afforded by the fixed-dose combination lercanidipine–enalapril.

Key words: Combination, Enalapril, Hypertension, Kidney, Lercanidipine, Renal protection

INTRODUCTION

Hypertension is a major risk factor for stroke, acute coronary events and chronic renal failure (1-5). The worldwide prevalence of hypertension ranges from approximately 25% in the general population to over double this figure in elderly individuals (6-9). These poor figures are mainly attributed to lack of adherence to both antihypertensive drug therapies and lifestyle recommendations (10, 11). Among the many factors that contribute to poor compliance, the side effect profile of drugs is probably the most influential.

In light of the need to attain blood pressure (BP) goals, both European guidelines and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) currently recommend combination therapy, especially when monotherapy fails to reach BP goals or in patients at high cardiovascular (CV) risk (1-3). The main advantages of combined therapy are (i) improved antihypertensive efficacy from combining 2 mechanisms of action; (ii) reduced incidence of side effects, due to lower doses administered; (iii) greater levels of compliance, due to fixed-dose regime and potential availability of single pill and (iv) reduced time required to attain BP targets (1). It is recognized that a range of fixed-dose antihypertensive therapies are currently available in clinical practice. These include angiotensin receptor blockers (ARBs) plus hydrochlorothiazide (HCTZ), angiotensin-converting enzyme (ACE) inhibitors plus HCTZ, β-blockers plus HCTZ, and calcium channel blockers (CCBs) plus ACE inhibitors (12, 13). However, these combinations are not always interchangeable, because many do not share similar tolerability and safety profiles or are not freely available in all countries. Of the various combinations available, CCBs and ACE inhibitors have been proven to be extremely effective, while also displaying good tolerability (14-24). Furthermore, in accordance with recent guidelines, this combination is specifically recommended for priority use in hypertensive patients (3). The association of a CCB and an ACE inhibi-