CHAPTER I

INTRODUCTION

Enalapril is an orally active angiotensin converting enzyme inhibitor which lack of a sulfhydryl (-SH) group and has little pharmacological activity until it was hydrolyzed to its active metabolised enalaprilat.[1-2] This drug cause blood pressure reduction in normotensive individuals and hypertensive patients and also produce favorable hemodynamic effects in patients with congestive heart failure mainly by suppressing the renin–angiotensin–aldosterone system.[3] In open and placebo–controlled studies in patients with mild to severe essential hypertension, enalapril 10 to 40 mg/day reduces both systolic and diastolic blood pressure about 15 to 20 %, with adequate pressure control being achieved in about 50 to 75 % of patients on enalapril alone.[4] Several large studies have defined efficacy of enalapril in less severe degrees of heart failure and in asymptomatic left ventricular dysfunction. These results have extended the earlier definition of signicantly reduced mortality during use of enalapril to treat severe heart failure[5-9].

Despite extensive clinical experience with enalapril, there is still controversy about optimal dosage regimens with this drug and others drugs in this class for starting dose, maintenance dose and frequency of administration.[10-11] Almost all the ACE inhibitors in clinical development have been examined over a wild range of doses, and the initial recommended dose range almost invariably has been scaled down after further experience in clinical practice. From these previous studies Arzilli

et al. have found that enalapril when given acutely to renovascular patients exerted a dose–dependent antihypertensive effect.[12] However later studies shown that, the antihypertensive effect of enalapril chronically given to essential hypertensive patients and measured at 24-hour after the dose showed flat dose–response curve with a major antihypertensive effect at 10 mg daily and a small added effect at 40 mg daily.[13]

Ambulatory blood pressure monitoring is now used widely to assess the efficacy of antihypertensive drugs in daily life conditions. These 24–hour measurements have a number of advantages compared to conventional sphygmomanometric readings.[14-16] Although a small placebo effect is observed in the first few hours after placebo administration, 24 – hour average blood pressure is substantially devoid of any placebo effect. Moreover, ambulatory blood pressure is not affected by the alerting reaction usually observed during the doctor's visit. When the 24–hour average value is considered, ambulatory blood pressure is more reproducible than clinic blood pressure. Finally, these observations are important clinically, since several studies have suggested that the risk of hypertensive cardiovascular complications (including both the development and regression of left ventricular hypertrophy) correlates more closely with 24-h or daytime ambulatory monitoring than with the office pressure[17-19]. Subtle functional abnormalities, however, have been found in white-coat hypertensives, including reduced compliance and increased mass of the left ventricle.

Since ambulatory blood pressure monitoring offer the possibility of obtaining reliable, reproducible and detailed information on the time-course and magnitude of the effect of antihypertensive treatment over 24 hours, the purpose of this present

study was to investigate the dose and blood pressure control of enalapril by using 24-hour non-invasive ABPM in patients with mild and moderate essential hypertension.

Objectives

1. To compare the 24-hour antihypertensive effects between different doses of enalapril in mild and moderate hypertensive patients.
2. To compare the 24-hour antihypertensive effects of enalapril at the same dose between mild and moderate hypertensive patients