Indian J Physiol Pharmacol 1996; 40(1): 83-86

EFFECTS OF ENALAPRIL ON LIPID PROFILE IN DIABETIC AND NON-DIABETIC ESSENTIAL HYPERTENSIVE PATIENTS

MILAN C. SATIA*, MAHESH L. SHUKLA AND RAMESH K. GOYAL**

**Department of Pharmacology,
L.M. College of Pharmacy,
Ahmedabad - 380 009
and
Shukla General Hospital,
Gandhi Road, Bardoli - 394 602

(**Received on February 14, 1995**)

Abstract : Effectiveness of enalapril was studied in hypertensive patients with or without diabetes-mellitus. All the patients received enalapril, 5-20 mg per day for 9 months. Enalapril effectively controlled the blood pressure and favourably altered the lipid levels and did not affect the glucose level in diabetics as well as non-diabetics. Enalapril may be considered as a better therapeutic option for the treatment of hypertension associated with diabetes mellitus.

Key words: enalalpril essential hypertension diabetes-mellitus

INTRODUCTION

Some of the available antihypertensive drugs are reported to affect lipid levels and worsen glycemic control. Thiazide diuretics are known to produce an adverse effect on plasma lipids (1) and also impaired glucose tolerance (2). Six months treatment with atenolol was found to decrease insulin sensitivity and this was accomplished by significant increase in fasting insulin levels, blood glucose and glycosylated haemoglobin (3). Atenolol has also been shown to increase triglyceride levels and decrease HDL-cholesterol levels in diabetic as well as non-diabetic hypertensive patients (4). Comparable data to guide on the suitability of these drugs is scanty. In a new therapeutic approach to the treatment of hypertension, the ideal agent should not only be efficacious and well-tolerated but also should reverse hypertension induced cardiovascular disease and should induce positive alteration of serum lipids. The present study was undertaken to investigate the effects of enalapril on lipid levels and other biochemical parameters in diabetic hypertensive and non-diabetic hypertensive patients.

METHODS

The study was an open clinical trial. It was approved by the local Ethical Committee.

Qualifying Criteria : Patients of either sex between 45-70 yrs in age, having body weight within 15-25% of ideal weight, visiting Shukla Hospital's OPD with a mean diastolic blood pressure of more than 90 but less than 110 mm Hg after 2-4 weeks of placebo treatment were included in the study. Patients were excluded if they had any severe retinopathy, cardiac, renal or neurological diseases to avoid the interaction of other drugs with the test drug.

Treatment period and protocol : The selected patients from hospital's OPD were fully explained about the procedures and a written consent was taken from them. Patients who met eligibility criteria were admitted to Shukla General Hospital for one day, and underwent thorough clinical examination and received

* *Present address : R&D Department of Pharmacology, Cadila Laboratories Limited, Ahmedabad - 380 008*
**Corresponding Author

placebo treatment for 2-4 weeks. For follow up, patients attended the OPD of Shukla Hospital.

Diabetic patients were maintained on their usual diet and oral antidiabetic treatment for the control of diabetes. At the end of placebo period, if they still met qualifying requirements, both non-diabetic essential hypertensive (EH) and diabetic hypertensive (DM-HT) patients received enalapril, 5 mg/day. After 4 weeks of active treatment, patients whose mean diastolic blood pressure was less than 90 mm/Hg were instructed to continue taking the same dose (5 mg/day enalapril). The dose of enalapril was increased by 5 mg every 2 weeks until blood pressure control (DBP < 90 mmHg and SBP < 145 mmHg) was achieved. The maximum dose of enalapril was increased upto 20 mg/day. Patients were evaluated every month and their blood pressure, heart rate and body weight were recorded at each visit.

Two other group of patients were also included in the study. The first group was non-hypertensive patients with non-insulin dependent diabetes mellitus (NIDDM) and second group was uncontrolled hypertensive (UN-HT) patients who had not taken antihypertensive medication regularly and came to the hospital with 200 mmHg/120 mmHg systolic blood pressure (SBP) and diastolic blood pressure (DBP) respectively.

At each visit, blood pressure recording was done using a Sphygmomanometer on the same arm and, whenever possible, by the same nurse or physician.

Laboratory investigations were performed at the end of the placebo period and after 3 months and 9 months of active therapy in DM-HT and EH groups. In NIDDM and UN-HT groups laboratory investigations were performed at the time of selection of patients. Twelve hours fasting blood samples were obtained for determination of blood glucose levels, serum cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, creatinine and urea levels. All biochemical analysis were performed by using commercial diagnostic kits.

No specific dietary prescription was provided to avoid diet fluctuation. Patients were required to continue their usual diet habits throughout the study. Patients were asked not to make changes in physical exercise or smoking habits during the course of the study. Drug compliance was assessed by pill counts.

Statistical analysis was performed using one way analysis of variance. A value of P less than 5% ($P<0.05$) was considered as significant.

RESULTS

Baseline demographics : Out of 78 patients, 20 (12 males and 8 females) had only non-insulin dependent diabetes mellitus (NIDDM); 18 (11 males and 7 females) had uncontrolled hypertension (UN-HT); 22 (12 males and 10 females) had NIDDM with hypertension (DM-HT); 20 (12 males and 8 females) were non-diabetic patients with essential hypertension (EH). A total of six patients were withdrawn from the study, 3 of DM-HT group and 3 of EH group who received enalapril. Two of them were withdrawn because of severe cough and other 4 did not have regular follow-up.

Blood pressure level : Enalapril administration in 19 diabetic hypertensive patients reduced both SBP and DBP from 178 ± 2.4/104 ± 1.5 mmHg to 142 ± 2.8/86 ± 2.3 mmHg respectively. The reduction in B.P. was observed after one month and it was found to be maintained upto 9 months of the study. In the group of 17 EH patients also the mean blood pressure was found to be significantly reduced from 170 ± 2.5/101 ± 2.1 mmHg to 138± 2.1/88 ± 1.7 mmHg ($P<0.05$). The patients with SBP less than 145 mmHg and DBP less than 90 mmHg throughout the 9 months therapy were considered to have controlled blood pressures. The blood pressure control by enalapril was found to be 84.2% in diabetic hypertensive patients and 75.5% in EH patients during 9 months of therapy.

Lipid profile : The lipid levels were adversely altered in NIDDM as well as UN-HT

patients. The total cholesterol levels were found to be 6.25 mmol/L and 6.61 mmol/L in NIDDM and UN-HT patients respectively. Triglyceride levels were found to be 2.0 and 2.57 mmol/L respectively. LDL-cholesterol levels were also found adversely altered. It was found to be 4.14 mmol/L and 4.27 mmol/L in NIDDM and UN-HT patients respectively. HDL-cholesterol were found on lower side in both the groups of patients. It was 1.25 mmol/L and 1.3 mmol/L in NIDDM and UN-HT patients respectively.

Enalapril therapy favourably altered the lipid profile in DM-HT and EH patients respectively. In both groups the total cholesterol, triglycerides and LDL-cholesterol were significantly decreased with 9 months enalapril treatment as compared to initial level, i.e. after 2-4 weeks placebo period (Fig. 1 and Fig. 2).

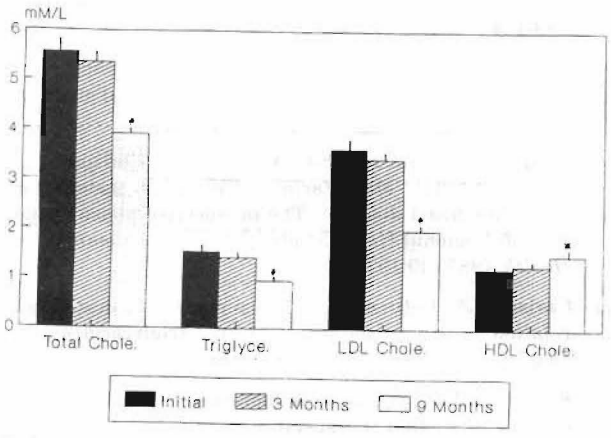

Fig. 1 : Effect of enalapril treatment for 9 months on lipid profile in diabetic hypertensive patients. Each point represents mean ± SEM of 19 patients. (*) denotes significant differance (P<0.05) from initial value.

Other biochemical parameters : Enalapril treatment did not alter glucose levels during 9 months therapy in EH and DM-HT patients as evaluated by fasting blood glucose levels. Serum creatinine and blood urea levels were also not affected significantly in both the groups of the patients throughout the 9 months therapy.

Side effects : Enalapril was well tolerated in both, DM-HT and EH group of patients. Out

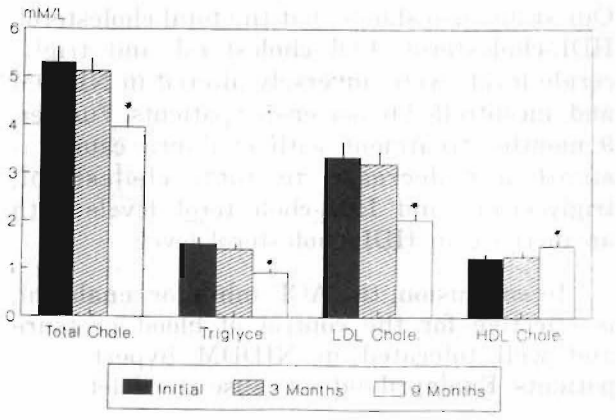

Fig. 2 : Effect of enalapril treatment for 9 months on lipid profile in essential hypertensive patients. Each point depicts mean ± SEM of 17 patients. (*) denotes significant (P<0.05) difference from initial value.

of 36 patients who received enalapril, 4 patients suffered from mild cough and 1 patient developed hyperkalemia. An increase in serum creatinine and blood urea levels were observed in 4 diabetic hypertensive patients and 3 non-diabetic hypertensive patients.

DISCUSSION

A single daily dose of enalapril effectively controlled blood pressure in 84.2% of DM-HT patients and 75.5% of EH patients for 9 months without causing any serious side effects or alteration of fasting blood glucose levels. The results of this study are in accordance with other reports that show enalapril to be an efficient antihypertensive agent (5, 6) and confirm previous observations showing that ACE inhibition is effective in the control of blood pressure in NIDDM hypertensive patients (7, 8). In diabetics, the use of ACE inhibitors is desirable as an alternative to diuretics and beta-blockers, which are known to impair glucose tolerance (2, 3).

The association of total cholesterol levels with the incidence of coronary heart disease is well established (9, 10). The positive relation between plasma triglyceride concentration and coronary events has also been reported (11-14).

Our study also shows that the total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride levels were adversely altered in NIDDM and uncontrolled hypertensive patients. Further, 9 months' treatment with enalapril caused a significant decrease in total cholesterol, triglyceride, and LDL-cholesterol levels with an increase in HDL-cholesterol level.

In conclusion, the ACE inhibitor, enalapril, is effective for the control of blood pressure and well tolerated in NIDDM hypertensive patients. Enalapril did not cause any deleterious influence on glucose levels but instead, improved lipid profile. Thus, enalapril may be a good therapeutic option for the treatment of hypertension when it is associated with diabetes-mellitus.

ACKNOWLEDGMENTS

This work was supported by a research grant from Council of Scientific and Industrial Research, New Delhi which is sincerely acknowledged.

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