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Research Article

Effects of angiotensin converting enzyme inhibitor: ramipril on different biochemical parameters in essential hypertensive patients

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ABSTRACT

Background: Hypertension is a major risk factor for macrovascular diseases. The beneficial effects of lowering blood pressure on the vascular morbidity and mortality are well documented and demonstrated. The beneficial effects of antihypertensive agents on cardiovascular system can be counter-balanced by the induction of metabolic disorders. The modifications in various metabolic parameters (like lipids, serum electrolytes, uric acid, blood glucose levels, etc) are responsible for different adverse drug reactions of antihypertensive drugs. It might also have potential to produce secondary morbidities after long term use. The present study was designed to evaluate the effect of the commonly used first line antihypertensive drugs on these different biochemical parameters. Recent comparative studies suggest that, for the prevention of cardiovascular events, angiotensin converting enzyme inhibitor (ACEI) may be superior to alternative antihypertensive agents, independently of their antihypertensive effect and also claimed to have neutral or favourable effects on carbohydrate metabolism, lipid profile, uric acid. The metabolic abnormalities can be improved by ACEI. Therefore, this study was conducted to evaluate the effects of ramipril on different biochemical parameters in essential hypertensive patients. Objective was to study effects of six months monodrug therapy with ramipril on different biochemical parameters in essential hypertensive patients.
Methods: 30 newly diagnosed patients of either gender with essential hypertension were included in the study. Patients having co-morbidities like diabetes mellitus, hyperlipidemia, gout, pregnant females were excluded from the study. Baseline readings of lipid profile, serum electrolytes, fasting blood sugar and uric acid were recorded before starting ramipril drug therapy. Same biochemical tests were repeated after six months ramipril monodrug treatment.
Results: After comparing the means there is significant decrease in triglyceride levels, highly significant decrease in LDL, uric acid, sodium and fasting sugar level and highly significant increase in HDL levels.
Conclusions: Ramipril has beneficial effects on RAS (Renin angiotensin system) and kinin system or both may contribute to the improvement in different biochemical parameters by ramipril.

Keywords: Biochemical parameters, Essential hypertension, Ramipril

INTRODUCTION

Hypertension is considered as a metabolic syndrome which affects many systems of the body and alters various biochemical parameters.[1] It is a leading cause of death worldwide and a major risk factor for cardiovascular diseases. Hypertension has long being called" the silent killer" because of its asymptomatic nature, although it is a condition that can be identified easily and treated effectively. Angiotensin converting enzyme inhibitors (ACEIs) like ramipril have been long in use for treating essential hypertension. Various studies

carried out with ramipril showed no significant changes in the biochemical parameters. However, there have also been some studies which have shown significant favourable changes in the various parameters. Therefore the present study was designed to observe the effect of ramipril on different biochemical parameters in essential hypertension. Ramipril is a lipophilic prodrug with active metabolite ramiprilate. It is comparatively long acting ACEI, given once a day. It shows good patient compliance and least side effects so accepted as monotherapy to which 50% of the population responds. ACEIs are first line drugs in all grades of hypertension (JNC-7) and also show neutral or favorable effect on carbohydrate metabolism and lipid profile.

METHODS

It is an open, prospective study conducted in OPD of medicine department of 50 beds multi-speciality private hospital in western Maharashtra. 30 patients [17 females (age group - 25 to 70 years) & 13 males (age group- 23 to 66)] newly diagnosed with mild to moderate hypertension were enrolled after informed & written consent was taken. Before administering the drug, baseline blood pressure and the biochemical parameters like lipid profile, serum electrolytes (sodium, potassium, and calcium), uric acid, fasting blood sugar level were recorded. 12-14 hrs overnight fasting blood sample was taken for laboratory investigation. Monotherapy with ramipril (Dose range- 1.25 to 5 mg OD) was started and follow up for checkup on blood pressure was carried out every month. The same biochemical parameters were measured after six months of mono drug ramipril therapy. Institutional ethics committee approval (KIMS/ETHICAL COM/2008 dt 26/10/2008) was taken prior to the initiation of the study. Study protocol and informed consent form were also approved by the ethics committee.

The patients included in the study were newly diagnosed patients as per JNC-7 stage I and II of essential hypertension without comorbities, who were above 18 years of age and of either gender.

The patients who were excluded from the study were the ones administered with hypolipidaemics, hypoglycemics, uricosurics, combination antihypertensive treatments, chronic drug therapy, steroids and estrogen or subjects with any hepatic or renal diseases or with a history of chronic smoking and chronic alcoholism. Pregnant, lactating and females on contraceptives were also excluded from the study.

Student's paired t test was applied for statistical analysis of the data. The data was expressed mean±SD and students paired t test was used for intra group comparison. $p<0.05$ was considered as statistically significant.

RESULTS

In the present study it was observed that there was significant decrease in TG and LDL cholesterol, significant increase in HDL cholesterol whereas decrease in TC and VLDL was not significant. Also there was significant decrease in serum sodium level, which was within normal limits and no significant change in potassium and calcium level was observed. There was statistically significant decrease in serum uric acid level and fasting blood sugar level.

Table 1: Effect of ramipril on lipid profile.

Parameters		Before Mean ± Std. dev	After Mean ± Std. dev	P value
Lipid Profile (mg/dl)	TC	182.6300± 26.1900	178.8300± 23.8200	0.1090
	TG	120.6700± 17.1100	116.2300± 14.6500*	0.0240
	HDL	43.7700± 7.1300	47.6300± 8.0000*	0.0010
	LDL	114.8300± 23.1100	107.9000± 18.0500*	0.0090
	VLDL	24.0330± 3.4490	23.2670± 2.9700	0.0650

Student's paired t-test: *p < 0.05

Table 2: Student's paired t-test: *p < 0.05.

Parameters		Before Mean± Std. dev	After Mean ± Std. dev	P value
Electrolytes (mEq/L)	Na^+	139.9000± 4.5890	138.3000± 3.1200*	0.0110
	K^+	4.1567± 0.4099	4.0967± 0.2918	0.4070
	Ca^{++}	9.7133± 0.5231	9.6833± 0.5325	0.5330
BSL (mg/dl)		79.3700± 8.3400	76.4300± 8.2400*	0.0060
Uric Acid (mEq/L)		4.1130± 0.6790	3.7230± 0.5290*	0.0000

Student's paired t-test: *p < 0.05

DISCUSSION

Effect on lipids

Three randomized, controlled trials detected small but statistically significant changes in total cholesterol, low density lipoprotein (LDL) 4 and TG levels.[2,3] Pollare et al, have evaluated in their study that hypertensive patients who were kept on ACEI captopril, showed a decrease in the serum cholesterol. In another study, statistically significant improvement in lipids was observed due to ACEI as compared to ARBs.[5,6] This conclusion

completely supports our results in which lipid levels were decreased.

ACE inhibitors might be effective in prevention of endothelial dysfunction, progression of atherosclerosis and coronary artery events by blocking the production of aldosterone and by blocking conversion of angiotensin I to angiotensin II. ACEI improved blood values of HDL cholesterol, which protect the artery from excessive accumulation of cholesterol.[7]

Effect on serum uric acid

Schmidt A et al, observed that uric acid levels were decreased by ACEI enalapril in hypertensive renal transplant recipients.[8] Weinberger MH, demonstrated in two multicenter trials that ACEI could prevent hydrochlorthiazide induced changes in uric acid levels.[9] ACEIs like captopril, enalapril and ramipril have been found to increase uricosuric effect by lowering the net reabsorption of UA in the proximal tubule.10 Present study results are in line with these findings.

Several evidences suggested that uric acid is responsible for the BP elevation and for the tubulointerstitial injury. Both angiotensin II and NO are involved in the pathogenesis of the hypertension and renal disease induced by uric acid. Various studies showed that blocking angiotensin II formation with ACEI and stimulating NO synthesis with L-arginine were able to largely prevent the hypertensive and renal changes.[11,12]

Effect on blood sugar levels

There are a number of findings in animal as well as clinical experimental studies and also in diabetic patients (with and without reduced renal impairment), which show that ACEIs show favourable effects on glucose.[13-16] The present study is in line with above findings as ramipril was seen to significantly decrease BSL.

The favourable effects on BSL may be indicated by the fact that by ACE inhibition, the increase in endogenous kinins may contribute to the improvement in insulin sensitivity. Increase in skeletal muscle blood flow and glucose uptake and increase in pancreatic blood flow, all probably contribute to the prevention of diabetes mellitus.

Effect on electrolytes

In a study by Fogari et al, showed ACEI mono therapy in hypertensives there was small but statistically significant increase in serum potassium.[17] Another author concluded that in absence of renal insufficiency, azotemia or congestive heart failure hyperkalemia is unusual.[18] Study by Weinberger MH, showed that no change in serum potassium was seen in the groups receiving captopril alone.[9] In the present study, ramipril significantly decreased sodium levels by 1% and showed non-significant changes in the levels of potassium and calcium

CONCLUSION

Besides lowering blood pressure, ramipril seems to have neutral/favourable effect on biochemical parameters, inducing minimal changes in serum electrolytes and decreasing incidences of new onset of diabetes. It might be of great value in prevention of CHD in hypertensive patients by improving coronary calcification and progression of atherosclerosis which predisposes to essential hypertension. Thus, the metabolic effect of antihypertensive drugs could be of special importance in long term treatment of essential hypertension. It suggests that ACEI (Ramipril) is an attractive option for treatment of hypertension as well as hypertension associated with hyperuricemia, gout, hyperlipidemia, type II diabetes patients and in patients with metabolic syndrome.

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