Original Article

Biochemistry

Efficacy Evaluation of Pharmaceutical Optimized Ramipril 1.25mg (F-4) with Essential Hypertension

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ABSTRACT

Introduction: Hypertension is one of the strongest modifiable risk factors for cardiovascular and kidney disease and has been identified as the leading risk factor for mortality. ACE inhibitors or angiotensin converting enzyme inhibitors reduce peripheral vascular resistance via blockage of the angiotensin converting enzyme. This action reduces the myocardial oxygen consumption.

Objective: This study aimed to evaluate the efficacy of once-daily optimized Ramipril 1.25mg (F-4) versus placebo.

Study design: placebo-controlled, comparative study

Place and Duration of Study: This study was conducted in the department of Biochemistry, University of Karachi from January 2010 to June 2010.

Methods: This was multicenter, randomized, placebo-controlled, comparative study. Patients were selected from different hospitals of Orangi Town Karachi and study was conducted in the department of Biochemistry, University of Karachi. Patients were randomized to receive optimized Ramipril 1.25mg (F-4) once daily and Placebo once daily for 8 weeks. The efficacy variable was change from baseline at the end of study which was evaluated.

Results: The patients treated with optimized Ramipril 1.25mg tablet (F-4) alone, blood pressure reduction was lower, although significant; reaching values of 139.9 ± 11.3 / 89.9 ± 5.5 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment.

Conclusion: The results of this study demonstrated that the optimized Ramipril 1.25mg (F-4) has a high antihypertensive efficacy and achieve desired blood pressure for eight weeks.

Key Words: Optimized Ramipril (F-4), hypertension, systolic blood pressure.

INTRODUCTION

Hypertension is one of the strongest modifiable risk factors for cardiovascular and kidney disease and has been identified as the leading risk factor for mortality[1].In European countries the prevalence of hypertension in adults is estimated to be approximately 44%[2]Angiotensin converting enzyme inhibitors have been shown to block the activation of the renin-angiotensin system in the plasma as well as in the vascular wall. Recent experimental and human data suggest that angiotensin converting enzyme inhibitors reduce proliferation of vascular smooth muscle; enhance endogenous fibrinolysis; have the potential to stabilize plaques; and decrease angiotensin II mediated atherosclerosis, plaque rupture, and vascular occlusion [3].Ramipril is a 2-aza-bicyclo [3.3.0]-octane-3-carboxylic acid derivative. It is a white, crystalline substance soluble in polar organic solvents and buffered aqueous solutions. Its empiric formula is C23H32N2O5, and its molecular weight is 416.5. ACE inhibitors, or angiotensin converting enzyme inhibitors (i.e. Enalapril, Ramipril, Captropril) reduce peripheral vascular resistance via blockage of the angiotensin converting enzyme. This action reduces the myocardial oxygen consumption, thereby improving cardiac output and moderating left ventricular and moderating left ventricular and vascular hypertrophy. ACEIs are recommended in current clinical practice guidelines for secondary prevention in patients with cardiovascular disease[4, 5]

Comparative safety and efficacy trials indicate that angiotensin receptor blockers like olmesartanme-doxomil have superior tolerability and antihypertensive efficacy[6]. Similar investigation using olmesartan, medoxomil and amlodipine besylate showed great effectiveness and tolerance in patient with hypertension[7]. Combination therapies reduced B.P to a greater extent than with amlodipine besylate alone as indicated with benazepril hydrochloride with valsartan and with perindopril[8,9.]

Therefore, the objective of this comparative study evaluating the efficacy of pharmaceutical optimized Ramipril 1.25mg (F-4) with placebo in the treatment of patients with essential hypertension..

MATERIALS AND METHODS

This was multicenter, randomized, placebo-controlled, comparative study. Patients were selected from different hospitals of Orangi Town Karachi from January 2010 to June 2010 and study was conducted in the department of Biochemistry, University of Karachi. Patient was randomized to receive optimized Ramipril 1.25mg (F-4) once daily and Placebo once daily for 8

weeks. The analysis of antihypertensive efficacy of a therapeutic regimen in the long term becomes important. The primary efficacy variable was change from baseline in MSDP at the end of study. Secondary variable was change in mean sitting systolic blood pressure from baseline.

RESULTS

The patients treated with optimized Ramipril 1.25mg tablet (F-4) alone, blood pressure reduction was lower, although significant; reaching values of 139.9 ± 11.3 / 89.9 ± 5.5 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment.

Table No.1: Baseline Characteristics

	Ramipril (F-4) (n=80)	Placebo (n=20)
Age (years)	50.2 ± 9.3	51.5 ± 9.8
Male / Female (%)	43.4 / 56.6	35.0 / 65.0
Body weight (Kg)	68.9 ± 13.5	71.2 ± 12.2
BMI (kg/m2)	27.5 ± 3.8	27.8 ± 3.4
SBP sitting (mmHg)	149.5 ± 11.5	148.8 ± 10.9
DBP sitting (mmHg)	95.7 ± 7.4	94.9 ± 7.8

Table No.2: Ambulatory Blood Pressure Monitoring. Mean Values of Blood Pressure

	Ramipril (F-4) (n=80	Placebo (n=20)	*P-value*
Systolic BP - 24 hours (mmHg)			
Baseline	147.8 ± 11.2	149.2 ± 11.5	NS
Week 8	139.9 ± 11.3	148.9 ± 11.2	0.0019
Diastolic BP - 24 hours (mmHg)			
Baseline	96.6 ± 7.4	94.4 ± 8.8	NS
Week 8	89.9 ± 5.5	93.9 ± 7.9	0.0094

NS: Non significant, p: probability

DISCUSSION

The baseline characteristics of the population included in the study are shown in Table no1. We can observe that the groups were not different in relation to age, body mass index and weight, heart rate, and systolic and diastolic pressure values .No significant variations of blood glucose and different parameters of lipid profile were observed during the eight-week of treatment with any of the three antihypertensive regimens used. Thus, the drug regimens used may be considered neutral as regards glucose, plasma lipid metabolism. The results of this study showed that the optimized product Ramipril 1.25mg (F-4) has a high antihypertensive efficacy that is sustained in the long term with a quite reduced percentage of loss of blood pressure control in table No.2 We observed that more than 70.8% of the patients treated with optimized product of Ramipril 1.25mg (F-4) remained with diastolic blood pressure levels equal to or lower than 90 mmHg, thus achieving the goals for the treatment of hypertension. The difficulty to achieve the goal of controlling systolic blood pressure explains why the international guidelines for studies on antihypertensive drugs still use criteria based on diastolic blood pressure to describe the antihypertensive efficacy of a drug, in spite of the fact that guidelines indicate the real need to control systolic blood pressure as well. It is important to point out that blood pressure reduction provided by the treatment with optimized product of Ramipril 1.25mg (F-4) did not cause any secondary Increase in sympathetic activity, since no significant variations of heart rate occurred. · Treatment with the ACE inhibitorramipril reduced cardiovascular mortality and morbidity in abroad range of patients at high risk for cardiovascular events.[10]In addition to a high efficacy in reducing blood pressure, keeping it at controlled levels, an antihypertensive drug should also have a good biochemical profile, since the presence of adverse effects may decrease the degree of compliance of the patient to the therapeutic regimen, thus ultimately leading to treatment dropout. Our results showed that the optimized product of Ramipril 1.25mg (F-4) at low doses has a very good biochemical profile with a low incidence of adverse events. The good biochemical profile of the optimized Ramipril 1.25mg (F-4) may be explained by the use of lower doses of each of the hypotensive drugs, since the existence of a strong relation between the dose of the hypotensive drug and the frequency of adverse events is known. However, some drugs used in the treatment of hypertension, such as diuretics and beta-blockers, are known to be able to promote harmful alterations in lipid metabolism, especially in glucose metabolism. In our study we observed that the use of the optimized Ramipril 1.25mg (F-4) did not change parameters of either glucose metabolism or plasma lipids, thus having a neutral biochemical profile even when used for 8 weeks. Based on these results we can suggest that the optimized product Ramipril 1.25mg (F-4) is safe and adequate for the treatment of hypertension in patients with metabolic syndrome, diabetes mellitus and dyslipidemias.

CONCLUSION

In brief, the results of this multicenter study demonstrated that the optimized Ramipril 1.25mg (F-4) has a high antihypertensive efficacy, allowing approximately 70.8% of the patients treated to achieve and maintain for eight weeks. We can suggest that the high antihypertensive efficacy, good tolerability and no biochemical effects of the optimized Ramipril 1.25mg (F-4) it is an excellent option for the treatment of hypertension.

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