Original Article

Effect of Lisinopril in Hypertension

Placebo- Controlled Trial of Pharmaceutical Optimized Lisinopril 10mg (F-5) in Patients with Essential Hypertension for Efficacy & Biochemical Evaluation

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ABSTRACT

Objective: The objective of this double-blind, randomized placebo-controlled trial study evaluating efficacy and biochemical effects of optimized lisinopril 10mg (F-5) as compared to placebo in adult patients with essential hypertension.

Study Design. Double-blind, randomized placebo-controlled trial

Place and Duration of Study: This study was conducted at the Department of Biochemistry, University of Karachi from October 20 11 to January 2012.

Materials and Methods: Patients were randomized to receive once optimized lisinopril 10mg (F-5) daily and Placebo once daily for 8 weeks and at the end of study efficacy and biochemical evaluation was done.

Result: The patients treated with optimized lisinopril 10mg (F-5) alone, blood pressure reduction was lower, although significant; reaching values of 140.1 ± 11.4/ 87.7 ± 5.4 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. .No significant variation of blood glucose was observed and different parameters of lipid profile were also observed during the eight weeks of treatment with antihypertensive regimen used. Thus, the drug regimens used may be considered neutral as regards glucose and plasma lipid metabolism profile because drug used at low doses.

Conclusion: We can suggest that the high antihypertensive efficacy, good tolerability and no biochemical effects of the optimized Lisinopril 10mg (F-5) it is an excellent option for the treatment of hypertension in a wide range of hypertensive patients, with a high potential to reduce cardiovascular risks.

Key Words: Hypertension, Lisinopril, Biochemical Effects

INTRODUCTION

Adequate blood pressure is a treatment of hypertension and it is the risk of cardiovascular morbidity and mortality so proper therapy is essential. And the reduction of blood pressure lower than 130/85 mmHg provides additional benefits regarding both protection of organs and cardiovascular mortality. Guidelines of World Health Organization for the treatment of hypertension that is, 130/85 mmHg which is lower than the previous limit of 140/90 mmHg.[1-6]

Blood pressure is an important modifiable risk factor for the progression of renal disease.[7] of all antihypertensive agents; inhibitors of angiotensin-converting enzyme (ACE) are regarded as particularly effective in limiting renal-disease progression , because of possible beneficial influences on kidney function, which are separate from the effects on systemic blood pressure.ACE inhibitors significantly limit the progression of renal disease in patients with macroalbuminuria,[7] and, at the time our trial was designed, there were indications that this beneficial effect also occurred in patients with micro-albuminuria.[8,9] If ACE inhibitors can slow the relentless decline of renal function in patients with microalbuminuria, it is reasonable to investigate whether use of ACE inhibitors in patients with normoalbuminuria may also be beneficial. However, previous trials of ACE inhibitors in normoalbuminuric patients are few, [10] and have either lacked power or have not been designed as randomized and controlled. [10, 11] consequently, the degree of albuminuria at which treatment with ACE inhibitors should start is unclear.

Lisinopril is one of the most widely used angiotensin-converting enzyme (ACE) inhibitors in adult medicine, and ACE inhibitors (ACE-Is) are a major component of cardiovascular therapy because of their beneficial effects on cardiac function in heart failure and myocardial infarction.[12,13] ACE-Is are particularly effective antihypertensive agents. In most hypertensive pediatric patients, especially younger patients, hypertension is secondary to renal disease and isrenin-mediated with activation of the renin- angiotensin system (RAS). Therapy with an ACE-I is therefore the first choice of drug in the pediatric population. The ability of ACE-Is to block the renin-angiotensin-aldosterone system (RAAS) accounts for their effect in reducing blood pressure (BP) but also prevents the deleterious effects of Ang II on endothelial function.

Lisinopril has been shown to decrease urinary protein excretion in adults with diabetes mellitus.[14]

Comparative safety and efficacy trials indicate that angiotensin receptor blockers like olmesartan medoxomil have superior tolerability and antihypertensive efficacy[15]. Similar investigation using olmesartan, medoxomil and amlodipine besylate showed great effectiveness and tolerance in patient with hypertension[16]. Combination therapies reduced B.P to a greater extent than with amlodipine besylate alone as indicated with benazepril hydrochloride with valsartan and with perindopril[17, 18]

Therefore, the objective of this comparative study evaluating the efficacy and biochemical effects of optimized Lisinopril 10mg (F-5) with placebo in the treatment of patients with essential hypertension.

MATERIALS AND METHODS

This was multicenter, randomized, placebo-controlled, comparative study. Patient was randomized to receive optimized Lisinopril 10mg (F-5) once daily and Placebo once daily for 8 weeks. The study was conducted in Department of Biochemistry, University of Karachi from October 20 11 to January 2012. Patients were selected from four different hospitals of orange Town and 80 patients were selected for the study. Therefore 80 patients were effectively analyzed for efficacy and tolerability the analysis of antihypertensive efficacy and biochemical effects 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. Safety biochemical parameters (complete blood count, renal function, liver function, electrolytes, protein profile, and enzymes) and electrocardiogram at rest were also determined in all patients at the baseline (week O) and at the 8th week of antihypertensive treatment. At the same time points, glucose metabolism parameter values and plasma lipids (total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglycerides) were also recorded. Biochemical parameters were determined using an automated method.

RESULTS

The patients treated with optimized Lisinopril 10mg (F-5) alone, blood pressure reduction was lower, although significant; reaching values of 140.1 ± 11.4 / 87.7 ± 5.4 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. Variations in blood pressure measurement in the standing position during treatment were similar to those recorded in the sitting position, and no episode of orthostatic hypotension was reported in either of the therapeutic regimen. No significant variation in leg volume measurement was observed among the both groups studied during the eight weeks of treatment. No significant variations of blood glucose were observed and different parameters of lipid profile were also observed during the eight weeks of treatment with antihypertensive regimen used. Thus, the drug regimens used may be considered neutral as regards glucose and plasma lipid metabolism profile because drug used at low doses.

Table No.1: Baseline characteristics

	Lisinopril 10mg(F-5) (n=60)	Placebo (n=20)
Age (years)	51.2 ± 9.4	51.5 ± 9.8
Male / Female (%)	40.4 / 59.6	35.0 / 65.0
Body weight (Kg)	69.9 ± 13.5	70.2 ± 12.2
BMI (kg/m2)	27.4 ± 3.6	27.8 ± 3.4
SBP sitting (mmHg)	149.9 ± 11.2	148.7 ± 10.7
DBP sitting (mmHg)	96.7 ± 7.3	95.9 ± 7.5

Table No.2: Ambulatory blood pressure monitoring. Mean values of blood pressure

	Lisinopril 10mg (F-5) (n=60)	Placebo (n=20)	P-value
	Systolic BP - 24 hours (mmHg)		
Baseline	149.9 ± 11.2	148.7± 10.7	NS
Week 8	140.1 ± 11.4	148.9± 11.3	0.0037
	Diastolic BP - 24 hours (mmHg)		
Baseline	96.7 ± 7.3	95.9 ± 7.5	NS
Week 8	87.7 ± 5.4	94.9 ± 7.8	0.0001

NS: Non significant, p: probability

Table No.3: Baseline Biochemical characteristics

	Lisinopril 10mg (F-5) (n=60)	Placebo (n=20)
	Fasting Blood Glucose(mg/dl)	
Baseline	99.4 ± 11.3	98.1 ± 8.7
Week 8	98.5 ± 11.7	97.9 ± 9.5
	Total Cholesterol (mg/dl)	
Baseline	197.9 ± 43.2	194.2 ± 33.4
Week 8	198.2 ± 43.4	193.9 ± 34.2
	LDL - Cholesterol (mg\dl)	
Baseline	114.4 ± 33.2	118.3± 25.8
Week 8	114.9 ± 33.5	117.8 + 24.7
	HDL - Cholesterol (mg\dl)	
Baseline	53.9 ± 13.2	47.9 ± 11.6
Week 8	52.8 ± 12.8	47.7 ± 11.5
	Triglycerides (mg\dl)	
Baseline	137.8 ± 88.7	145.6 ± 88.2
Week 8	137.1 ± 89.2	144.2 ± 88.9

DISCUSSION

Hypertension is a major risk factor for stroke. In relation to other stroke-specific factors, brain tissue loss as a consequence of stroke has been associated with cognitive impairment; these strokes may be isolated or

strategically located ones (e.g. in the thalamus, angular gyrus, frontal white matter).[19] Also, because hypertension often does not exist as a solitary factor but occurs in the presence of other metabolic risks, other stroke-related factors such as inflammation or abnormal insulin signaling in the brain, or the presence of metabolic syndrome could exist and underlie cognitive impairment or dementia in persons with hypertension.[20, 21]

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. The results of this study showed that the optimized product Lisinopril 10mg (F-5) as 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 69.2% of the patients treated with optimized product of Lisinopril 10mg (F-5) 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 Lisinopril 10mg (F-5) did not cause any secondary Increase in sympathetic activity, since no significant variations of heart rate occurred. Our results showed that the optimized product of Lisinopril 10mg (F-5) at low doses has a very good biochemical profile with a low incidence of adverse events. The good biochemical profile of the optimized Lisinopril 10mg (F-5) 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 Lisinopril 10mg (F-5) did not change parameters of either glucose metabolism or plasma lipids, thus having a neutral biochemical profile even when used for 8 weeks. Table.No.3 Based on these results we can suggest that the optimized product Lisinopril 10mg (F-5) is safe and adequate for the treatment of hypertension in patients with metabolic syndrome, diabetes mellitus and dyslipidemias .Incidentally, hypertension is frequently associated to the metabolic syndrome; also, the frequency of this association increases with age.

CONCLUSION

In brief, the results of this multicenter study demonstrated that the optimized Lisinopril 10mg (F-5) has a high antihypertensive efficacy, allowing approximately 69.2% 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 Lisinopril 10mg (F-5) it is an excellent option for the treatment of hypertension.

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