Original Article

Effects of Anti-Hypertension Drug

Efficacy & Biochemical Evaluation of Pharmaceutical Optimized Valsartan 80mg (F-3) with Essential Hypertension

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ABSTRACT

Objective: The objective of this double-blind, comparative study evaluating efficacy and biochemical effects of optimized Valsartan 80mg (F-3) as monotherapy in adult patient with essential hypertension.

Study Design. Double-blind, comparative study

Place and Duration of Study: This study was conducted at the Department of Biochemistry, University of Karachi from January 2011 to September 2011.

Materials and Methods: This was multicenter randomized, double-blind, comparative study. Patients were randomized to receive once Valsartan (F-3) daily for 8 weeks and at the end of study efficacy and biochemical evaluation was done.

Results: The patients treated with optimized Valsartan 80mg (F-3) alone, blood pressure reduction was lower, although significant; reaching values of 140.9 ± 11.3 / m88.9 ± 5.5 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 Valsartan 80mg (F-3) 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, Valsartan, Biochemical effects

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] Current guidelines for the management of hypertension recommend a target blood pressure of 140/90 mmHg, with a stricter target for patients who have a high risk of cardiovascular events (< 130/80 mmHg).[3,4] Valsartan can control blood pressure for 24h,[5] probably because of its highly selective blockade of the AT1 receptor. In addition, when the AT1 receptor is blocked by an ARB and unbound Ang II can bind the AT2 receptor, the stimulation of the AT2 receptor may be involved in the effects of the ARB. The stimulation of AT2 receptors mediates natriuresis, which may contribute to the antihypertensive effect[6]. Interestingly, the local application of valsartan by means of valsartan-eluting stents inhibits neointima formation and increases AT2 receptor mRNA expression after vascular injury in a rabbit model, suggesting that up-regulation of the AT2 receptor by valsartan plays an important role through its antiproliferative effect.[7]Comparative safety and efficacy trials indicate that angiotensin receptor blockers like olmesartan medoxomil have superior tolerability and antihypertensive efficacy[8]. Similar investigation using olmesartan, medoxomil and amlodipine besylate showed great effectiveness and tolerance in patient with hypertension[9]. Combination therapies reduced B.P to a greater extent than with amlodipine besylate alone as indicated with benazepril hydrochloride with valsartan and with perindopril[10,,11.] The angiotensin-receptor blocker (ARB) valsartan and the calcium-channel blocker (CCB) amlodipine have proven to be safe and effective antihypertensive agents when used as monotherapy.[12–15] Therefore, the objective of this comparative study evaluating the efficacy and biochemical effects of optimized Valsartan 80mg (F-3**)** 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 Valsartan 80mg (F-3) once daily and Placebo once daily for 8 weeks. The study was conducted in Department of Biochemistry, University of Karachi from January 2011 to September 2011, Patients were selected from four different hospitals of orange Town and 80 patients were selected for the study. Therefore 80patients 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 Valsartan 80mg (F-3) alone, blood pressure reduction was lower, although significant; reaching values of 140.9 ± 11.3 / m88.9 ± 5.5 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.

Table No.1: Baseline characteristics

	Valsartan (F-3) (n=60)	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

	Valsartan (F-3) (n=60)	Placebo (n=20)	P-value
Systolic BP - 24 hours (mmHg)			
Baseline	149.8 ± 11.2	149.2 ± 11.5	NS
Week 8	140.9 ± 11.3	148.9 ± 11.2	0.0074
Diastolic BP - 24 hours (mmHg)			
Baseline	97.6 ± 7.4	95.4 ± 8.8	NS
Week 8	88.9 ± 5.5	94.9 ± 7.9	0.0003

NS: Non significant, p: probability

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.3: Baseline Biochemical characteristics

	Valsartan (F-3) (n=60)	Placebo (n=20)
Fasting Blood Glucose (mg/dl)		
Baseline	97.4 ± 11.5	99.1 ± 8.8
Week 8	95.5 ± 11.9	98.9 ± 9.2
	Total Cholesterol (mg/dl)	
Baseline	197.2 ± 43.2	195.2 ± 33.3
Week 8	199.7 ± 43.5	193.9 ± 34.1
	LDL - Cholesterol (mg\dl)	
Baseline	114.4 ± 34.1	117.9 ± 25.9
Week 8	114.9 ± 34.5	116.8 + 24.7
	HDL - Cholesterol (mg\dl)	
Baseline	52.9 ± 13.1	48.9 ± 11.7
Week 8	51.8 ± 12.8	48.7 ± 11.5
	Triglycerides (mg\dl)	
Baseline	137.2 ± 88.5	145.5 ± 88.1
Week 8	136.1 ± 89.3	144.2 ± 88.9

DISCUSSION

The baseline characteristics of the population included in the study are shown in Table No 1. 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 Valsartan 80mg (F-3) 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 71.8% of the patients treated with optimized product of Valsartan 80mg (F-3) 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 Valsartan 80mg (F-3) did not cause any secondary Increase in sympathetic activity, since no significant variations of heart rate occurred. 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 Valsartan 80mg (F-3) at low doses has a very good biochemical profile with a low incidence of adverse events. The good biochemical profile of the optimized Valsartan 80mg (F-3) 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 Valsartan 80mg (F-3) 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 Valsartan 80mg (F-3) is safe and adequate for the treatment of hypertension in patients with metabolic syndrome, diabetes mellitus and dyslipidemias. Because alterations in these parameters are very frequently observed in hypertensive patients. Incidentally, hypertension is frequently associated to the metabolic syndrome; also, the frequency of this association increases with age. 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. Based on these results we can suggest that this therapeutic modality is safe and adequate for the treatment of hypertension in patients with metabolic syndrome, diabetes mellitus and dyslipidemia.

CONCLUSION

In brief, the results of this multicenter study demonstrated that the optimized Valsartan 80mg (F-3) has a high antihypertensive efficacy, allowing approximately 71.8% 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 Valsartan 80mg (F-3) it is an excellent option for the treatment of hypertension.

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