Original Article

Biochemistry

Evaluation of Efficacy & Biochemical Effects of Pharmaceutical Optimized Amlodipine 5mg (F-5) with Essential Hypertension

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ABSTRACT

Introduction: An 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. Amlodipine is a calcium channel-blocking agent with vasodilator activity without side effects.

Objective: This study aimed to evaluate the efficacy and safety profiles of once-daily optimized amlodipine 5mg (F-5) versus placebo.

Study Design: Multicenter, randomized, placebo-controlled, comparative study

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

Materials and Methods: This was multicenter, randomized, placebo-controlled, comparative study. Patients were randomized to receive optimized Amlodipine 5mg (F-5) once daily and Placebo once daily for 8 weeks. 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. Biochemical effects were evaluated at the end of study from baseline.

Results :In the patients treated with optimized Amlodipine 5mg (F-5) alone, blood pressure reduction was lower, although significant, reaching values of 138.2 ± 10.9 / 88.4 ± 6.5 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. No significant variations of blood glucose and different parameters of lipid profile were observed during the eight-week of treatment. Thus, the drug regimen used may be considered neutral as regards glucose, plasma lipid metabolism.

Conclusion: We can suggest that the high antihypertensive efficacy, good tolerability and no biochemical effects of the optimized Amlodipine 5mg (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: Optimized Amlodipine, hypertension, tolerability, systolic blood pressure.

INTRODUCTION

An 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 chlorophenyl)-1, 4- significantly lower than the previous limit of 140/90 mmHg.[1-6]

Amlodipine besylate is chemically 3-ethyl 5-methyl 2-(2-aminoethoxymethyl)-4-(2-dihydro-6-methyl pyridine -3, 5-dicarboxylate monobenzenesulfonate. It is a calcium channel-blocking agent with vasodilator activity[7].Amlodipine is a peripheral arterial vasodilator that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure. It may be used alone or in combination with other antihypertensive agents. With chronic once daily oral administration, antihypertensive effectiveness is maintained for at least 24 hours and is well tolerated as monotherapy and in combination with other drugs without orthostatic hypotention[8]. It has a long elimination half-life making it suitable for once daily dosing confirmed by intra-arterial ambulatory blood pressure monitoring[9].The most common solid dosage forms in contemporary practice are tablets, which may be defined as "Unit forms of solid medicaments prepared by compaction". Most consists of a mixture of powders which has been compacted in a die to produce a single rigid body[10]

Amlodipine is a peripheral arterial vasodilator that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure. It may be used alone or in combination with other antihypertensive agents. With chronic once daily oral administration, antihypertensive effectiveness is maintained for at least 24 hours and it well tolerated as monotherapy and a combination with other drugs without orthostatic hypotension [11]. It has alone

elimination half-life making it suitable for once -daily dosing confirmed by intra-arterial ambulatory blood pressure monitoring [12]. .Stability studies of amlodipine besylate in two liquid dosage forms ;one in 1% methyl cellulose in syrup (1;0 and another in equal volumes of ora plus, showed 905 physical and chemical stability of its initial concentration[13].Despite the availability of numerous antihypertensive agents patients with patients with hypertension fail to achieve the blood pressure goal, therefore require multihpertensive therapy. A patient-related factor likely to effect adherence to treatment is the convenience of the prescribed drug regimen and was studied in antihypertensive therapy with fixed dose Amlodipine/Benazepril versus comparable component based therapy[14-15].Similar investigation using olmesartan,medoxomil and amlodipine showed great effectiveness and tolerance in patient with hypertension[16].

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

MATERIALS AND METHODS

This was multicenter, randomized, placebo-controlled, comparative study. Patients were randomized to receive optimized Amlodipine 5mg (F-5) once daily and Placebo once daily for 8 weeks. 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. Biochemical effects were evaluated at the end of study from baseline.

RESULTS

In the patients treated with optimized Amlodipine5mg (F-5) alone, blood pressure reduction was lower, although significant, reaching values of 138.2 ± 10.9 / 88.4 ± 5.3 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. 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.

Table No.1:Baseline Characteristics

	Amlodipine (F-5) (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 1± 1.5	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

	Amlodipine(F-5) (n=80)	Placebo (n=20)	P-value
	Systolic BP - 24 hours (mmHg)		
Baseline	149.5 ± 11.5	148.8 ± 10.9	NS
Week 8	138.2 ± 10.9	147.2 ± 11.3	0.0014
	Diastolic BP - 24 hours (mmHg)		
Baseline	95.7 ± 7.4	93.4± 8.8	NS
Week 8	88.4 ± 6.5	92.1 ± 7.9	0.0318

NS: Non significant, P: probability

Table No.3: Baseline characteristics

	Amlodipine (F-5) (n=80)	Placebo (n=20)	P-Value
	Fasting blood glucose(mg/dl)		
Baseline	97.4 ± 10.5	96.9 ± 8.8	
Week 8	95.5 ± 10.9	97.1 ± 9.2	NS
	Total Cholesterol (mg/dl)		
Baseline	193.9 ± 42.9	194.3 ± 32.9	
Week 8	197.8± 43.5	193.9 ± 32.7	NS
	LDL - cholesterol (mg\dl)		
Baseline	112.9± 32.9	117.1 ± 24.2	
Week 8	117.8 ± 33.2	116.8 ± 24.5	NS
	HDL - Cholesterol (mg\dl)		
Baseline	52.1 ± 12.9	49.2 ± 12.3	
Week 8	52.2 ± 11.8	49.5 ± 12.2	NS
	Triglycerides (mg\dl)		
Baseline	137.2 ± 89.1	143.2 ± 87.8	
Week 8	135.8± 88.9	143.9 ± 87.7	NS

NS: Non significant

DISCUSSION

The baseline characteristics of the population included in the study are shown in Table I. 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. Biochemical effects on glucose and lipid - Glucose and plasma lipid metabolism parameter values assessed at the baseline and at the 8th week of treatment are shown in Table No.3.The results of this study showed that the optimized product Amlodipine 5mg (F-5) has a high antihypertensive efficacy that is sustained in the long term with a quite reduced percentage of loss of blood pressure control. We observed that more than 70.8% of the patients treated with optimized product of Amlodipine 5mg (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 Amlodipine 5mg (F-5) 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 Amlodipine 5mg (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 Amlodipine 5mg (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. We evaluate biochemical effects especially glucose and lipids.

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. The pharmacological agents of the class of calcium channel antagonists, in turn, have a neutral metabolic profile. Amlodipine, a calcium antagonist, has proved its effectiveness in the treatment of primary hypertension in monotherapy and in association with other antihypertensive drugs [11]. A trend was detected toward reduced progression of atherosclerosis with amlodipine vs. placebo in the Comparison of Amlodipine versus Enalapril to Limit Occurrences of Thrombosis (CAMELOT) trial [17]. However, calcium channel blockers have no effect on secondary prevention of CAD.

In our study we observed that the use of the optimized Amlodipine 5mg (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. Based on these results we can suggest that the optimized product Amlodipine 5mg (F-5) 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 Amlodipine 5mg (F-5) has a high antihypertensive efficacy, allowing approximately 72.3% 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 Amlodipine 5mg (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.

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