Original Article

Biochemical Effects of Drugs with Hypertension

Evaluation of Efficacy & Biochemical Effects of Amlodipine / Atorvastatin with Essential Hypertension

1. Asnad 2. Abdul Latif Ansari 3. Ruqia Fida 4. Muhammad Ishaq 5. Israr Ahmed Akund

1. Asstt. Prof. of Biochemistry 2. Assoc. Prof. of Pathology, 3. Asstt. Prof. of Gynaecology 4. Prof. of Surgery 5. Prof. of Physiology, Jinnah Medical College, Peshawar

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. Combination therapy of amlodipine plus atorvastatin improved vascular compliance, an indicator of structural and functional vascular changes, and the beneficial effect on small arteries appeared to be more than additive.

Objective: This study aimed to evaluate the efficacy and biochemical effects of once-daily optimized Amlodpine/Atorvastatin 5/10 mg (F-6) versus placebo.

Study Design: placebo-controlled, comparative study

Place and Duration of Study: This study conducted in the Department of Biochemistry, University of Karachi from July 2010 to January 2011.

Materials and Methods: This was multicenter, randomized, placebo-controlled, comparative study. Patients were selected from different hospitals of Orangi Town Karachi and samples were analyzed in the department of Biochemistry, University of Karachi. Patients were randomized to receive optimized Amlodpine/Atorvastatin 5/10 mg (F-6) once daily and Placebo once daily for 8 weeks. The efficacy & biochemical effects variables were change from baseline at the end of study which was evaluated.

Results: In the patients treated with optimized Amlodipine /Atorvastatin 5/10mg tablets` (F-6) alone, blood pressure reduction was lower, although significant, reaching values of 136.9 ± 10.7 / 88.2 ± 6.3 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. Thus, the drug regimens used may be considered neutral as regards glucose and significantly reduce LDL-Cholesterol.

Conclusion: Due to the high antihypertensive efficacy and hypolipidemic and no biochemical effects of the optimized Amlodipine/Atorvastatin 5mg (F-6) it is an excellent option for the treatment of hypertension and hyperlipidemia patients, with a high potential to reduce cardiovascular risks.

Key Words: Optimized Amlodipine/Atorvastatin 5mg (F-6) ,Hypertension, Hyperlipidemia.

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 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[7].After oral ingestion of Atorvastatin, this is an inactive lactone, is hydrolyzed to corresponding ortho-hydroxy acid leading to the inhibition of 3-hydroxy 3-methyl glutaryl – coenzyme A. (HMG- CoA) reductase, responsible for catalyzing the conversion of HMG CoA to mevalonate, which is an early and rate limiting step in cholesterol biosynthesis[8]. Hypertension and dyslipidemia are two of the most commonly co-occurring cardiovascular risk factors. Combination therapy of amlodipine plus atorvastatin improved vascular compliance, an indicator of structural and functional vascular changes, and the beneficial effect on small arteries appeared to be more than additive [9, 10]

The objective of this comparative study evaluating the efficacy and biochemical effects of optimized Amlodpine/Atorvastatin 5/10 mg (F-6) with placebo in the treatment of patients with essential hypertension and hyperlipidemia.

MATERIALS AND METHODS

This was multicenter, randomized, placebo-controlled, comparative study. Patients were selected from different hospitals of Orangi Town Karachi from July 2010 to January 2011 and samples were analyzed in the department of Biochemistry, University of Karachi. Patient was randomized to receive optimized Amlodopine/Atorvastatin 5/10mg (F-6) 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 Amlodipine /Atorvastatin 5/10mg tablets` (F-6) alone, blood pressure reduction was lower, although significant, reaching values of 136.9 ± 10.7 / 88.2 ± 6.3 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. No significant variation of blood glucose was observed during the eight-week of treatment with antihypertensive regimens used. Thus, the drug regimens used may be considered neutral as regards glucose and significantly reduce LDL-Cholesterol.

Table No.1: Baseline Characteristics

	Amlodipine/ Atorvastatin (F-6) (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)	148.5 ± 10.5	149.8 ± 10.9
DBP sitting (mmHg)	96.7 ±7.4	95.9 ± 7.8

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

	Amlodipine/ Atorvastatin (F-6) (n=80)	Placebo (n=20)	*P-value*
	Systolic BP - 24 hours (mmHg)		
Baseline	148.5 ±10.5	149.8 ±10.9	NS
Week 8	138.2 ± 10.9	147.2± 11.3	0.0014
	Diastolic BP - 24 hours (mmHg)		
Baseline	96.7 ± 7.4	95.9 ± 7.8	NS
Week 8	88.4 ±6.5	92.1± 7.9	0.0318

NS: Non significant, P-value: probability value

Table No.3: Baseline of Biochemical Characteristics

	Amlodipine /Atorvastatin (F-6) (n=80)	Placebo (n=20)	*P-value*
	Fasting blood glucose(mg/dl)		
Baseline	98.7 ± 9.8	97.9± 9.4	NS
Week 8	97.2± 9.5	96.8± 9.3	NS
	LDL - cholesterol (mg\dl)		
Baseline	168.2 ± 13.2	167.5± 12.9	NS
Week 8	118.2± 14.2	165.5± 12.4	0.0001

NS: Non significant, P-value: probability value

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, The results of this study showed that the optimized product Amlodipine/ Atorvastatin 5/10mg (F-6) has a high antihypertensive efficacy and hypolipidemic activity that is sustained in the long term with a quite reduced percentage of loss of blood pressure control table no.2. Amlodipine has demonstrated some anti-atherosclerotic properties, whereas the beneficial effects of atorvastatin on atherosclerosis, via a reduction in cholesterol levels, are more marked[11].Hypertension is often associated with impaired fibrinolysis, usually expressed by increased levels of plasminogen activator inhibitor type 1 (PAI-1) and decreased activity of tissue plasminogen activator (t-PA).[12] Combination therapy with amlodipine and atorvastatin improved the fibrinolytic balance more than either single agent in hypertensive hypercholesterolemic patients with insulin resistance.[12] We observed that more than 50.2% of the patients treated with optimized product of Amlodipine/Atorvastatin 5/10mg (F-6) remained with diastolic blood pressure levels equal to or lower than 90 mmHg, thus achieving the goals for the treatment of hypertension and hyperlipidemia Table No.3. 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/Atorvastatin 5/10mg (F-6) 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/Atorvastatin 5/10mg (F-6) at low doses has a very good hypolipidemic activity and best antihypertensive effect with a low incidence of adverse events. The good biochemical profile of the optimized Amlodipine/ Atorvastatin 5/10mg(F-6) 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. . The pharmacological agents of the class of calcium channel antagonists, in turn, have a neutral metabolic profile. In our study we observed that the use of the optimized Amlodipine/Atorvastatin 5/10mg (F-6) did not change parameters of glucose metabolism thus having a neutral biochemical profile even when used for 8 weeks. Based on these results we can suggest that the optimized product Amlodipine/ Atorvastatin 5/10mg (F-6) is safe and adequate for the treatment of hypertension and hyperlipidemia

CONCLUSION

In brief, the results of this multicenter study demonstrated that the optimized Amlodipine/ Atorvastatin 5/10mg (F-6) has a high antihypertensive efficacy and hypolipidemic activity, allowing approximately 50.2% of the patients treated to achieve and maintain for eight weeks. We can suggest that the high antihypertensive efficacy and hypolipidemic and no biochemical effects of the optimized Amlodipine/ Atorvastatin 5mg (F-6) it is an excellent option for the treatment of hypertension and hyperlipidemia patients, with a high potential to reduce cardiovascular risks.

REFERENCES

1. Sykowsky PA, D'Agostino RB, Belanger AJ, Kannel WB. Secular Trends in Long Term Sustained Hypertension, Long Term Treatment and Cardiovascular Morbidity. The Framingham Heart Study 1950-1990. Circulation 1996;93:697-703.
2. MacMahon S, Peto R, Cutler J, et al. Blood Pressure, stroke, and coronary heart disease. Part 1, prolonged differences in blood pressure: prospective observational studies corrected for regression dilution bias. Lancet 1990;335:765-77.
3. IV Diretrizes Brasileiras de Hipertensão Arterial - Sociedade Brasileira de Hipertensão;Sociedade Brasileira de Cardiologia e Sociedade Brasileira de Nefrologia. Hipertensão 2003;5(4):126-63.
4. Chobaniam AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure-JNC 7. Hypertension 2003;42: 1206-52.
5. European Society of Hypertension - European Society of Cardiology guidelines for management of arterial hypertension. J Hypertens 2003;21: 1011-53.
6. Hansson L, Zanchetti A, Carruthers SG, Dahlof B, et al. On behalf of HOT Study group. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomized trial. Lancet 1998;351:1755-62.
7. Julius S. Amlodipine in hypertention. J. Cardiovasc. Pharmacol 1988;12:S27-S33.
8. Bays HE, Moore PB, Drehobl MA, et al. Effectiveness and tolerability of atorvastatin calcium in patients with primary hypercholesterolemia: pooled analysis of two phase II studies. Clin Ther 2001;23 (8):1209-1230.
9. Cohn J, Neutel J, Houston M, et al. Early improvements in vascular compliance following coadministration of amlodipine and atorvastatin in patients with concomitant hypertension and dyslipidemia. The Avalon Arterial Wall Compliance (AWC) trial. San Francisco, CA. Program and abstracts from the 20th Annual Scientific Meeting of the American Society of Hypertension; May 14–18; 2005.
10. Leibovitz E, Beniashvili M, Zimlichman R, Freiman A, Shargorodsky M, Gavish D. Treatment with amlodipine and atorvastatin have additive effect in improvement of arterial compliance in hypertensive hyperlipidemic patients Am J Hypertens 2003;16(9 Pt 1):715–718
11. Jukema JW, van der Hoorn JW. Amlodipine and atorvastatin in atherosclerosis: a review of the potential of combination therapy. Expert Opin Pharmacother 2004;5(2):459–468.
12. Fogari R, Derosa G, Lazzari P, et al. Effect of amlodipine-atorvastatin combination on fibrinolysis in hypertensive hypercholesterolemic patients with insulin resistance. Am J Hypertens 2004;17(9):823–827.

Address for Corresponding Author:
Prof. Dr. Muhammad Ishaq
Chairman & Founder
Jinnah Medical College, Peshawar
Cell: +92-333-9152060