Effect of amlodipine on serum lipid profile in hypertensive patients

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ABSTRACT

Objectives: To assess the effect of amlodipine, as monotherapy, in hypertensive patients, on serum lipid profile, as assessed by serum cholesterol, serum triglyceride, high density lipoprotein cholesterol (HDLC), and low density lipoprotein cholesterol (LDLC).
Subjects and methods: Thirty three hypertensive patients were included in the study, 25 of them were males and 8 were females. Serum cholesterol, triglyceride, HDLC and LDLC were measured before and after 2 months of starting treatment with amlodipine.
Results: No significant difference could be found between the pre and post treatment levels of all measured parameters.
Conclusion: Treatment with amlodipine does not produce deleterious effect on lipid profile, so it may be a suitable therapy in a hypertensive patient with underlying hyperlipidaemia.

الخلاصة

أهداف البحث: أجريت هذه الدراسة لتقييم تأثير عقار الاملودبين كعلاج أحادي لمرضى ارتفاع ضغط الدم الشرياني على مستوى الكولسترول، الدهون الثلاثية، البروتين الشحمي عالي الكثافة، والبروتين الشحمي منخفض الكثافة.
المشاركون وطرق العمل: أجريت الدراسة على ٣٣ مريضا مصابا بارتفاع ضغط الدم الشرياني، ٢٥ مريضا منهم من الذكور و ٨ من الإناث. تم قياس مستوى الكولسترول، الدهون الثلاثية، البروتين الشحمي عالي الكثافة، والبروتين الشحمي منخفض الكثافة قبل وبعد شهرين من بدء العلاج بعقار الاملودبين.
النتائـــج: أظهرت نتائج الدراسة عدم وجود فرق معنوي في مستوى القيم المقاسة قبل وبعد العلاج.
الاستنتاج: العلاج بواسطة عقار الاملودبين لايؤثر على مستوى الدهون في الدم وقد يكون علاجا مناسبا لمرضى ارتفاع ضغط الدم اللذين يعانون من اضطرابات في مستوى الدهون.

Arterial hypertension is one of the major risk factors for atherosclerosis and coronary artery disease, and its treatment has proved to be beneficial for preventing those pathologies. Because dyslipidaemia has been frequently associated with arterial hypertension, being also a strong risk predictor of coronary artery disease, one could assume that antihypertensive drugs should not have unwanted effects on lipid profile [(1)]. It has been suggested that the metabolic side effects of antihypertensive drugs are responsible for their failure to reduce cardiovascular morbidity in patients with hypertension. Treatment with some antihypertensive agents may cause unwanted changes in the lipid profile, attenuating their beneficial antiatherogenic effects of blood pressure reduction[(2)]. Beta blockers and thiazids may adversely affect the lipid profile and consequently increase the risk for coronary atherosclerosis [(3,4)]. On the other hand, angiotensin converting enzyme (ACE)

inhibitors, such as captopril, seem to have a neutral effect, or even improve lipid profile in hypertensive hypercholesterolaemic individuals[5]. Little information is available about the effect of calcium channel blockers, hence, the present study was undertaken to evaluate the effect of amlodipine, a long-acting dihydropyridine calcium channel blocker, on the serum lipid profile.

Patients and methods

This study was conducted from April to August 2007 on a number of hypertensive patients referred from their attending physicians. The inclusion criteria were as follows: newly diagnosed hypertensive patients who did not previously start any antihypertensive therapy. They should be free from other organic diseases especially hepatic and renal diseases. Patient with history of heart failure, ischemic heart diseases, diabetes as well as smokers and alcoholic were excluded from the study. Their treating physicians should decide that they need no other drug apart from the antihypertensive agent. Out of 66 patients, 47 met the above inclusion criteria and were included in this study.

Patients were instructed to continue the same diet which they were taking in the past 2 months prior to commencement of the study. Careful follow up made sure that no drug was added during the 2 months of the study; especially considering the last 2 weeks.

A total of 33 patients successfully completed the study. Out of these, 25 patients were males and 8 were females. The mean age of patients was 40.03 ± 7.63 years, with the range of 28 to 55 years. They received amlodipine as monotherapy in a mean dose of 7.27 ± 2.75 mg, ranging from 2.5-10 mg/day.

The lipid profile was done before starting the treatment and at the end of 2 months. The serum was collected in the morning after 14 hours fasting. Serum total cholesterol, triglycerides, and high density lipoprotein cholesterol (HDLC) were directly estimated. The low density lipoprotein cholesterol (LDLC) was calculated using Freidwald formula.

Paired t-test was used to compare the differences between the obtained values before and after treatment.

Results

The effect of amlodipine on the lipid profile of the patients has been shown in table (1). No significant difference could be found between the pre and post treatment levels.

Table (1): Effects of amlodipine on serum cholesterol, triglycerides, HDLC and LDLC.

Parameters	Before treatment Mean ± SD	After treatment Mean ± SD	P value
Total Cholesterol mg/dl	161.72 ± 27.15	160.45 ± 25.67	NS
Triglycerides mg/dl	115.72 ± 28.89	116.00 ± 28.25	NS
HDLC mg/dl	53.93 ± 3.23	54.06 ± 2.68	NS
LDLC mg/dl	84.48 ± 24.32	83.54 ± 22.60	NS

NS: not significant.

Discussion

The present study reveals no statistically significant alteration on either serum cholesterol, triglycerides, HDLC and LDLC levels.

The effects of antihypertensive drugs on lipid profile vary with both the pharmacological class and the individual drugs. Because adverse metabolic effects probably reduce the

benefit of blood pressure reduction therapy [6,7], many studies have examined the effects of different antihypertensive agents on lipid levels. Although there is a general consensus that thiazide diuretics and nonselective β-blockers adversely affect lipid levels, many areas of disagreement still exist about the effects of other antihypertensive agents on lipids. Most authors agree that alpha blockers reduce triglyceride levels, [8-12] and many authors have concluded that ACE inhibitors do not affect lipids [13-15].

The findings of the current study are in line with the results of other authors [16-19], as they all found that calcium antagonists as a group have no significant effects on lipids. This study prospectively evaluated the impact of amlodipine, as a relatively new calcium channel blocker, on lipid profile in hypertensive patients, as this drug is increasingly used in clinical practice.

Drug-induced changes in lipid levels may be particularly important in hypertensives, since up to 40 percent of untreated patients with essential hypertension and many patients with borderline hypertension already have lipid abnormalities [20]. The relative change in blood pressure and lipid levels may have different effects on cardiovascular risk, depending on baseline levels. Thus, a reduction in blood pressure in persons with severe hypertension may decrease risk substantially, even if lipids are adversely affected. Conversely, treating mild hypertension with agents that increase cholesterol levels may be counterproductive [21]. For the same amount of blood pressure reduction, agents that adversely affect lipids may cause less reduction in cardiovascular disease. Indeed, this may partially explain why trials with diuretics and β-blockers failed to reduce cardiovascular disease as much as would have been expected from the degree of blood pressure reduction[22]. Whether newer agents that reduce blood pressure without adversely affecting lipids will more favorably affect cardiovascular disease remains to be proven in controlled clinical trials. Meanwhile, the result of this study provides additional information suggesting that amlodipine has no effects on serum lipid profile.

In two similarly conducted studies (in Japan and Brazil), amlodipine did not influence plasma lipids adversely. In both studies, serum total, LDL, and HDL cholesterol were not altered, while serum triglycerides and VLDL cholesterol were significantly reduced. Similar beneficial effect on triglycerides level was not noticed in our study, however [23, 24].

Beyond the neutral effect of amlodipine on traditional serum lipid profile, a new study has shown that amlodipine significantly reduced oxidized LDL, an important atherogenic component of LDL [25].

Studies on rats provided additional favorable mechanism of amlodipine as a vasoprotective, beyond its blood pressure lowering effect; where two studies have shown that amlodipine does not only inhibit atherosclerotic plaque formation, but also regresses atherosclerosis. These effects are at least partly due to inhibition of oxidative stress and inflammatory response [26, 27] .

AVALON study[28] is a recent multicentre that confirmed the safety, effectiveness, and tolerability of amlodipine and atorvastatin given together as a single pill for the treatment of coexisting hypertension and hyperlipidaemia. This is considered the first version of a polypill to treat these two common disorders.

In conclusion: as far as serum lipid profile was concerned, amlodipine can be considered a safe antihypertensive drug in hypertensive patients with dyslipidaemia.

References

1. Kaplan NM. Treatment of hypertension: remaining issues after the Anglo-Scandinavian cardiac outcomes Trial. Hypertension 2006; 47: 10-13.
2. Krone w, Nagele H. Effects of antihypertensive on plasma lipids and lipoprotein metabolism. Am Heart J 1988; 116: 1729-1734.
3. Ames RP, Hill P. Raised serum lipid concentrations during diuretic treatment of hypertension: a study of predictive indexes. Clin Sci Mol Med Suppl. 1978; 4:311s-314s.

4. Leren P, Helgoland A, Holeme I, Foss PO, et al. Effect of propranolol and prazocin on blood lipids. Lancet 1980; 2: 4-6.
5. Ferrara LA, Marino LD, Russo O, et al. Doxazosin and captopril in mildly hypercholesterolemic hypertensive patients. The doxazosin- captopril in hypercholesterolemic hypertensive study. Hypertension 1993; 21: 97-104.
6. Stokes JD, Kannel WB, Wolf PA, Agostino RB, et al. Blood pressure as a risk factor for cardiovascular disease. The Framingham study-30 years of follow up. Hypertension 1989; 13(5 Suppl): 113-8.
7. Collins R, Peto R, MacMahon S, Hebert P, et al. Blood pressure, stroke, and coronary heart disease. Part 2, Short-term reductions in blood pressure: overview of randomized drug trials in their epidemiological content. Lancet 1990; 335:827-38.
8. Kannel WB, Carter BL. Initial drug therapy for hypertensive patients with hyperlipidemia. Am Heart J. 1989; 118:1012-21.
9. Lardinois CK, Neuman SL. The effects of antihypertensive agents on serum lipids and lipoproteins. Arch Intern Med. 1988; 148:1280-8.
10. Weidmann P, Ferrier C, Saxenhofer H, Uehlinger DE, et al. Serum lipoproteins during treatment with antihypertensive drugs. Drugs 1988; 35(Suppl 6):118-34.
11. Giles TD. Antihypertensive therapy and cardiovascular risk. Are all antihypertensives equal? Hypertension 1992; 19(1 Suppl):I124-9.
12. Grimm RH Jr. Antihypertensive therapy: taking lipids into consideration. Am Heart J. 1991; 122:910-8.
13. Ames RP. Antihypertensive drugs and lipid profiles. Am J Hypertens 1988; 1:421-7.
14. Ames RP. The effects of antihypertensive drugs on serum lipids and lipoproteins. I. Diuretics. Drugs. 1986; 32:260-78.
15. Black HR. Metabolic considerations in the choice of therapy for the patient with hypertension. Am Heart J. 1991; 121:707-15.
16. Chait A. Effects of antihypertensive agents on serum lipids and lipoproteins. Am J Med. 1989; 86(Suppl 1B):5-7.
17. Hunninghake DB. Effects of celipridol and other antihypertensive agents on serum lipids and lipoproteins. Am Heart J. 1991; 121: 696-701.
18. Raftery EG. The metabolic effects of diuretics and other antihypertensive drugs: a perspective as of 1989. Int J Cardiol. 1990; 28:143-50.
19. Verma RB, Chaudhary VK, Jain VK. Effect of calcium channel blockers on serum lipid profile. J Postgrad Med. 1987; 33(2): 65-68.
20. Julius S, Jamerson K, Mejia A, Krause L, et al. The association of borderline hypertension with target organ changes and higher coronary risk. Tecumseh blood pressure study. JAMA 1990; 264: 354.
21. Neaton JD, Wentworth D. Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316,099 white men. Multiple Risk Factor Intervention Trial Research Group. Arch Intern Med. 1992; 152:56-64.
22. MacMahon S, Peto R, Cutler J, Collins R, et al. Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. Lancet. 1990; 335:765-74.
23. Sanjuliana AF, Barraso SG, Fagundes VGA, Rodriguis MLG, Netto JF, et al. Moxonidine and amlodipine effects on lipid profile, urinary sodium excretion and caloric intake in obese hypertensive patients. Am L Hypertes 2000;13:620-8
24. Ahaneku JE, Sakata K, Urano T, Takada Y, Takada A. Lipids, lipoproteins, and fibrinolytic parameters during amlodipine treatment for hypertension. J Health Sc. 2000;46:455-8
25. Muda P, Kampus P, Teesalu R, Zimer K, Ristimäe T, Fischer K, et al. Effect of amlodipine and candesartan on oxidized LDL level in patients with mild to moderate

essential hypertension. Blood Press 2006;15:313-8
26. Toba H, Nakagawa Y, Milki S, Shimizu T, Yoshimura A, Inoue R, et al. Calcium channel blockades exhibit anti-inflammatory and oxidative effects by augmentation of endothelial nitric oxide synthase and inhibition of angiotensin converting enzyme in N(G)-nitro-L-arginine methyl ester- induced hypertensive rat aorta: vasoprotective effects of amlodipine and manidipine. Hypertens Res 2005;28(8):689-700.
27. Yoshii T, Iwai M, Li Z, Chen R, Ide A, Fukunga S, et al. Regression of atherosclerosis by amlodipine via anti-inflammatory and anti-oxidative actions Hypertens Res 2006;29(6):457-66
28. Messeri FM, Bakris GL, Ferrera D, Houston MC, Petrella RJ, Flack JM, et al. Efficacy and safety of co administered amlodipine and atorvastatin in patients with hypertension and dyslipidaemia; results of the AVALON trial. J Clin Hypertens (Greenwich) 2006;8(8):571-81.

