Proceeding S.Z.P.G.M.I. vol: 17(2): pp. 61-66, 2003.

To Study the Effects of Amlodipine (Calcium Channel Blocker) on Lipid Profile in Hypertensive Patients

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SUMMARY

Amlodipine belongs to the dihydropyridine subclass of calcium antagonist. It is a potent peripheral and coronary vosodilator with selectivity for vascular smooth muscle and minimal effect on myocardial contractility or cardiac conduction. Forty patients (20 male and 20 female) with mild or moderate essential hypertension were selected. Blood pressure was controlled in twenty-five patients with 5 mg dose of Amlodipine and in fifteen patients with 10 mg in twelve weeks. Serum Cholesterol, serum Triglycerides and serum Lipoprotiens (HDL, LDL) was carried out by Standard kit methods (Merck). Mean blood pressure of both male and female was significantly reduced. Present study observed non-significant variation in the mean values of serum triglyceride and serum HDL-Cholesterol and significant variation in the mean values of serum cholesterol and serum LDL- Cholesterol levels before and after Amlodipine treatment in male and female patients on either 5 mg or 10 mg of Amlodipine. It is therefore concluded that Amlodipine is an antihypertensive drug having some lipid lowering effects.

INTRODUCTION

Hypertension is the most common cardiovascular disease. Sustained arterial hypertension damages blood vessels in kidney, heart, and brain and leads to an increased incidence of renal failure, coronary disease, cardiac failure and stroke[1].

In more than 95 % of cases a specific underlying cause of hypertension cannot be found. Such patients are said to have essential hypertension. Effective pharmacologic lowering of blood pressure has been shown to prevent damage to blood vessels and to substantially reduce morbidity and mortality rates[2].

The concept of calcium antagonism or blocking of calcium channel as a specific mechanism of drug action was first reported[3] in 1967. The drugs (Calcium Channel Blockers) inhibited the Ca^{2+} component of ionic currents carried in the cardiac action potential. Because of this activity these drugs are also referred to as slow channel blockers, calcium channel antagonist and calcium entry blockers[4].

Amlodipine belongs to the dihydropyridine subclass of calcium antagonist. It is a potent peripheral and coronary vosodilator with selectivity for vascular smooth muscle and minimal effect on myocardial contractility or cardiac conduction[5].

It is very liposoluble molecule, which is well absorbed after oral administration; peak concentration in plasma is measured at 6-12 hours. The bioavailability of single oral dose is 65-90% and is not influenced with food. Amlodipine is highly metabolized in the liver (upto 90%) to inactive metabolites that are excreted in the urine[6].

Owing to the lipophilic character of Amlodipine, considerable concentrations occur in lipid containing membrane depots. The Amlodipine thus concentrated is slowly released from these depots and subsequently reach its target, the L-type calcium channels. This phenomenon explains both the slow onset and the long duration of action[7].

Amlodipine is effective and well tolerated in patients with mild or moderate hypertension as a single agent therapy[8], or in combination with other drugs[9]. It produces both peripheral arterial vasodilatation and coronary dilatation. However there is less reflex tachycardia with Amlodipine possibly because the long half-life produces minimal peaks and troughs in plasma concentration[10].

Amlodipine reduces the mean triglycerides and very low-density lipoproteins levels in

hypertensive patients with high baseline values of lipid profile while the changes in lipids and lipoproteins were not significant after Amlodipine treatment with medium baseline values of lipid profile[11]. It provided an additional benefit with decreased low-density lipoprotein cholesterol level[12].

Aims and objectives

To study the effects of amlodipine (Calcium Channel Blocker) on lipid profile in hypertensive patients.

PATIENTS AND METHODS

Forty patients with mild or moderate essential hypertension were selected. The diagnosis of essential hypertension was based on two separate blood pressure readings with a minimum interval of two weeks. If patients have been taking any medication that was with held for a wash out period of two weeks. The blood pressure at the end of two weeks wash out period was regarded as the base line value.

In this study twenty patients were females and twenty were male patients. Out of forty, eleven patients were newly diagnosed cases of hypertension, while twenty-nine were old hypertensives in whom two weeks wash out period was given. Blood pressure was controlled in twenty-five patients with 5 mg dose of Amlodipine and in fifteen patients with 10 mg. Serum Cholesterol, serum Triglycerides and serum Lipoprotiens (HDL, LDL) was carried out at 0 week and than after 12 weeks by Standard kit methods (Merck).

RESULTS

The values of the age and blood pressure at 0 week and after 12 weeks in both sexes were noted (Table 1). It was observed that the mean age of male patients was 52 years and of female patients was 48 years. Mean blood pressure at 0 week of male patients was 160/110mm/Hg and of female patients was 155/105mm/Hg. After 12 weeks of administration of amlodipine, mean blood pressure was significantly decreased ($P<0.001$) in both sexes.

The effects of amlodipine on serum cholesterol, serum triglycerides, serum lipopprotiens (HDL and LDL) and ratio of cholesterol:HDL cholesterol in male hypertensive patients was noted. (Table 2) It was observed that the mean serum cholesterol level was 227.85mg/100ml, before the administration of amlodipine (zero week). After six weeks it was significantly decreased ($P< 0.01$) when compared with zero week. After twelve weeks of administration of amlodipine it was also significantly decreased ($P<0.001$) when compared with zero week level of serum cholesterol. Mean serum Triglyceride level was 174.65mg/100ml, before the administration of amlodipine (zero week). After six weeks it was non-significantly decreased when compared with zero week level of serum Triglyceride. After twelve weeks of administration of Amlodipine it was further non-significantly decreased when compared with zero week as well as with six weeks level of Triglyceride. Mean serum LDL-Cholesterol level was 143.25mg/100ml before the administration of Amlodipine (zero week). After six weeks it was significantly reduced ($P< 0.001$) when compared with zero week level of serum LDL-Cholesterol. After twelve weeks it was further significantly reduced ($p< 0.001$) when compared with zero week level of serum LDL-Cholesterol. Mean serum HDL-Cholesterol level was 45.50mg/100ml before the administration of amlodipine (zero week). After six weeks it was same when compared with zero week level of serum HDL-Cholesterol. After twelve weeks the comparison was again non-significantly decreased when compared with zero week as well as with six weeks level of HDL-Cholesterol. Ratio of cholesterol:HDL cholesterol at zero week was 5.05mg/100ml. After twelve weeks of administration of amlodipine it was non-significantly decreased when compared with six weeks and as well as with zero week.

The effects of amlodipine on serum cholesterol, serum triglycerides, serum lipopprotiens (HDL and LDL) and ratio of cholesterol:HDL cholesterol in female hypertensive patients was noted. (Table 3) It was observed that the mean serum cholesterol was 211.20mg/100ml before the administration of amlodipine (zero week). After six weeks it was non-significantly reduced when compared with zero week level of serum cholesterol. After twelve weeks of administration of amlodipine it was significantly reduced ($P < 0.001$) when compared with zero week level of serum cholesterol. Mean serum Triglyceride level was 160.50mg/100ml before the administration of

Table 1: Age (years) and blood pressure (mmHg) in hypertensive male and female patients at (0 week) and after (12 weeks) with Amlodipine.

Values expressed as mean ± s.e.m. No of cases in parenthesis.

Parameters	Male (20)	Female (20)
Age (yrs)	52.50±2.39	48.9±2.40
Blood pressure (0 week)	160.00±2.42/110.00±1.16	155.00±2.45/105.00±1.98
Blood pressure (12 weeks)	130.00±2.02/80.00±0.97**	125.00±1.98/80.00±0.99**

**P<0.001=Highly significant difference

Table 2: Variation in the levels of serum Cholesterol, triglycerides and lipoprotiens (HDL and LDL) and ratio of cholesterol/HDL-cholesterol (mg/dl) before and after giving Amlodipine in male patients from 0-12 weeks

Values expressed as mean±s.e.m.

Period of study	Cholesterol (mg/dl)	HDL-cholesterol (mg/dl)	LDL-cholesterol (mg/dl)	Triglyceride (mg/dl)	Ratio of cholesterol/ HDL-cholesterol (mg/dl)
0 weeks	227.85±8.07	45.40±1.13	143.25±5.87	174.65±14.02	5.05±1.13
6 weeks	223.55±11.04*	45.20±1.18	136.30±7.36**	162.35±10.88	4.96±1.11
12 weeks	192.05±7.35**	43.15±1.06	111.15±5.67**	152.20±10.47	4.30±0.96

*P<0.01=Significant difference
**P<0.001=Highly significant difference

Table 3: Variation in the levels of serum Cholesterol, triglycerides and lipoprotiens (HDL and LDL) and ratio of cholesterol/HDL-cholesterol (mg/dl) before and after giving Amlodipine in female patients from 0-12 weeks

Values expressed as mean ± s.e.m.

Period of study	Cholesterol (mg/dl)	HDL-cholesterol (mg/dl)	LDL-cholesterol (mg/dl)	Triglyceride (mg/dl)	Ratio of cholesterol/ HDL-cholesterol (mg/dl)
0 weeks	211.20±7.59	43.30±1.20	135.70±7.95	160.50±13.99	4.90±1.09
6 weeks	197.00±6.2	42.50±1.24	126.80±4.75	147.40±11.42	4.80±1.07
12 weeks	184.65±6.58**	40.65±2.35	116.20±5.00*	136.57±10.85	4.50±1.00

*P<0.01=Significant difference
**P<0.001=Highly significant difference

amlodipine (zero week). After six weeks it was non-significantly decreased when compared with zero week level of serum Triglyceride. After twelve weeks of administration of amlodipine it was again non-significantly decreased when compared with zero week as well as with six weeks level of serum Triglyceride. Mean serum LDL-Cholesterol level was 135.70mg/100ml before the administration of Amlodipine (zero week). After six weeks it was non-significantly reduced. After twelve weeks it was further significantly reduced ($p<0.01$) when compared with zero week level of serum LDL-Cholesterol. Mean serum HDL-Cholesterol level was 43.30mg/100ml before the administration of amlodipine (zero week). After six weeks it was non-significantly reduced when compared with zero week level of HDL-Cholesterol. After twelve weeks it was also non-significantly reduced when compared with zero week as well as with six weeks level of HDL-Cholesterol. Ratio at zero week was 4.90mg/100ml. After six weeks of administration of Amlodipine it was non-significantlly reduced. After twelve weeks the ratio was again non-significantly reduced when compared with six weeks and as well as with zero week.

DISCUSSION

In this study we assessed the change in lipid profile before and after giving Amlodipine to hypertensive patients. Amlodipine (calcium channel blocker) is effective in mild to moderate hypertension as a single agent therapy or in

combination with other drugs by blocking L-type calcium channels leading to peripheral and coronary vasodilatation. The pharmacological properties of Amlodipine that may confer atheroprotection are calcium channel blockade, membrane modifier, antioxidant, and inhibition of gene expression. The antiatherosclerotic effect is mediated through a reduction in blood pressure and / or a decrease in vascular smooth muscle cell migration/proliferation along with a possible direct effect[13].

Present study observed non-significant variation in the mean values of serum triglyceride and serum HDL-Cholesterol and significant variation in the mean values of serum cholesterol and serum LDL- Cholesterol levels before and after Amlodipine treatment in male and female patients on either 5 mg or 10 mg of Amlodipine, is consistent with the previous findings by number of studies[11,14-21]. There were no significant sex differences for blood lipids ; however, there were greater decreases in serum cholesterol and LDL-Cholesterol levels in male patients than in female patients reason being that menopause appears to result in unfavourable changes in lipoprotein profiles[19] and in weight gain[22].

It is suggested that firstly, Amlodipine is markedly lipophilic allowing it to partition readily into cell membranes[23]. Secondly, in the membrane it has the ability to reorder or restore the swollen membrane bi-layer back to normal in atherosclerotic smooth muscle cells[24]. Thirdly, it has potent antioxidant properties[25]. Fourthly, it appears to inhibit the expression of variety of genes implicated in atherogenesis[26]. Fifthly, it is a calcium channel blocker[2]. Present study observed a reduction in blood pressure that was highly significant ($P < 0.001$) in 0-12 weeks with use of Amlodipine in both sexes. This reduction in blood pressure is explained by Benowitz[2] reason being that Amlodipine is a calcium channel blocker and it lowers blood pressure by relaxing arterioler smooth muscle cells and decreasing peripheral vascular resistance.

The potential benefit of Amlodipine is repoted in number of studies[2,8,16] in hypertensive population. Since hypertension is a virulent risk factor for large vessel disease, atheroprotective calcium channel blocker may have an added benefit in the therapeutic management of high blood pressure[27]. It is therefore concluded that Amlodipine is an antihypertensive drug having some lipid lowering effects. However a further study is needed to observe the influence of base line values on lipid and lipoprotein changes during Amlodipine treatment in hypertensive patients.

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