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Original research article

BENEFICIAL EFFECT OF LOW DOSE AMLODIPINE VS NIFEDIPINE ON SERUM CHOLESTEROL PROFILE OF RABBITS RECEIVING STANDARD DIET.

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ABSTRACT

Objective: To investigate the effect of low dose amlodipine v/s nifedipine on serum cholesterol profile of rabbits receiving standard diet. **Methods**: Fourty Newzealand rabbits were selected for the study. Their cholesterol profile was estimated at the beginning of the study. Rabbits were grouped into 4 groups receiving standard diet (control group), standard diet + vehicle propylene glycol, standard diet + nifedipine dissolved in propylene glycol and standard diet + amlodipine dissolved in propylene glycol. Along with standard diet they were treated with respective drugs for ten weeks. At the end of ten weeks serum cholesterol profile was estimated. **Results**: The cholesterol profile was estimated at the beginning and at the end of ten weeks. Total cholesterol in the amlodipine group decreased from 97±4.06 mg/dl to 90±4.2 mg/dl and HDL-Cholesterol increased from 32.01±4.40 mg/dl to 37±4.60 mg/dl after 10 week treatment but these changes were not significant. LDL cholesterol decreased significantly in rabbits with low dose of amlodipine from 55.42±3.32 mg/dl to 32.40±3.22 mg/dl and. In the nifedipine group there was a slight increase in total cholesterol from 102.49±5.16 mg/dl to 106±5.39 mg/dl, HDL cholesterol from 34.10±2.80 to 35.16±2.82 mg/dl and LDL cholesterol also increased from 56.20±2.20 mg/dl to 59.00±2.20 mg/dl after 10 week treatment. **Conclusion**: The study shows amlodipine produces favorable alterations in serum cholesterol profile.

Key words: Cholesterol profile, Standard diet, Amlodipine, Nifedipine

INTRODUCTION

Hyperlipidaemia and hypertension are often two co-existing risk factors for coronary artery disease. Among different cholesterol high serum levels of total cholesterol and low density lipoprotein cholesterol favours coronary artery disease. A report by the National cholesterol education program[11] has focused attention on the necessity for managing lipid disorders. Serum cholesterol plays a central role in the atherosclerotic process, in particular, abnormal levels of total cholesterol

and low – density lipoprotein cholesterol. High density lipoprotein particles function in the opposite way from low density lipoprotein, they act as a scavenger of free cholesterol and enhance the rate of clearance of cholesterol from the arteries.[3] It has been reported in a large number of animal and human experimental studies that various classes of antihypertensive agents have either adverse or significant, effect on plasma lipid & lipoprotein levels.[1,4,5] Beta-blockers without partial intrinsic sympathomimetic activity increase serum triglycerides and tend to lower high-density lipoprotein cholesterol.[9] Recently there has been an epidemical increase in hypertensive cases resulting in coronary artery disease and abnormal lipid profile. Therefore we planned in this study to see whether amlodipine versus nifedipine to test if this drug having antihypertensive effect in human, has any effect on serum cholesterol profile of rabbits fed on standard diet.

MATERIALS AND METHOD

Fourty healthy male Newzealand rabbits weighing between 2-3 Kg was selected and placed under ideal conditions. Animals were maintained on the routine standard feed and acclimatized for seven days prior to start of the experiment. Nifedipine (Pfizer Ltd): A solution of 5 mg/40ml in propylene glycol prepared and administered orally in a dose of 2ml/kg i.e. 0.25 mg/kg orally. Amlodipine (Pfizer Ltd): A solution of 2.5mg/40 ml in propylene glycol prepared and administered orally in a dose of 2ml/kg i.e. 0.125 mg/kg orally. Estimations of serum total cholesterol and serum high and low density lipoprotein cholesterol were done at the beginning of the study and after 10 weeks of administration of the study drugs.

Study design

The rabbits were divided into four groups containing 10 rabbits each. The groups were treated as follows:

Group I Standard diet (control group)

Group II Standard diet+ vehicle propylene glycol 2ml/kg/day

Group III Standard diet +Nifedipine (0.25mg/kg/day)

Group IV Standard diet +Amlodipine 0.125mg/kg/day orally

A routine diet containing bread, milk and vegetable on an average of 100gm/rabbit was given to the rabbits during the study period with water given ad-libitum. The animals were treated in this manner for 10 weeks. For analysis of cholesterol profile i.e. total cholesterol, HDL-cholesterol and LDL-cholesterol 1ml blood samples were collected from the marginal ear vein of rabbit after an overnight fast at the beginning before starting the drug administration and then after ten weeks of the drug administration. Readings were taken on a photo colorimeter. The data were analyzed using students paired 't' test for the same group and students unpaired t test for between the groups.

Table: 1. Cholesterol profile in the rabbits baseline values (Pretreatment)

Sr. No	Group	Total Cholesterol (mg/dl)	HDL-cholesterol (mg/dl)	LDL-cholesterol (mg/dl)
1.	Group I	95.00± 1.28	32.16± 2.08	56.55±3.72
2.	Group II	97.00± 1.28	34.01± 3.20	54.20± 5.20
3.	Group III	102.49± 5.16	34.10± 2.80	56.20± 2.20
4.	Group IV	97.00± 4.06	32.01± 4.40	55.42± 3.32*

Table: 2. Cholesterol profile in rabbits after 10 weeks of drug administration

Sr. No	Group	Total Cholesterol (mg/dl)	HDL-cholesterol (mg/dl)	LDL-cholesterol (mg/dl)
1.	Group I	99.00± 1.28	31.02± 2.08	53.12± 3.72
2.	Group II	100.00± 1.28	34.00± 3.20	55.00± 5.20
3.	Group III	106.00± 5.19	35.16± 2.82	59.00± 2.20
4.	Group IV	90.00± 4.06	37.00± 460.	32.40± 3.32*

The data were analyzed by paired 't' test ($p<0.001$)*LDL-C is decreased significantly in group 4 treated with amlodipine as compared to group 3 treated with nifedipine , control group1; 2 & pretreatment groups1, 2, 3 & 4.

RESULTS

The group 1 and 2 did not exhibit any significant alteration in serum cholesterol profile. There was a slight decrease in serum total cholesterol in the group-4 treated with amlodipine than non treated group 1, 2 & 4. But the mean serum total and LDL-C levels of the group 4 treated with amlodiine, rabbits were significantly reduced when compared to group 3 at tenth weeks.Thus amlodipine significantly prevented the rise of LDL-C($p<o.oo1$). There was a considerable rise in HDL-C in group 4 rabbits receiving amlodipine. The mean serum levels of HDL-C of group 3 & 4 rabbits receiving nifedipine & amlodipine respectively increased marginally after 10 weeks than basal groups.

DISCUSSION

Administration of amlodipine in group 4 resulted in significant lowering of LDL-C after 10 weeks when compared to group 3 rabbits receiving nifedipine. Similar effects of nicardipine in lowering LDL-C and elevating HDL-C has been reported by Ohata et al[12]. It is now well recognized that coronary artery disease bears a relationship through inter linkage between hypertension and dyslipidemia. The treatment of hypertension is found with potential difficulties, including the altered efficiency of medications, the increased risk of side effects and possibility for derangement of serum lipid levels. Serum cholesterol plays a central role in the atherosclerotic process, in particular, abnormal levels of total cholesterol, low density lipoprotein cholesterol and high density lipoprotein cholesterol have been found to be predictors of coronary heart disease risk in hypertension. As the major transport vehicles for cholesterol, low-density lipoprotein particles essentially deposit cholesterol in the lining of the arterial wall; low-density lipoprotein cholesterol is often referred to as bad cholesterol. High-density lipoprotein particles function in the opposite way from low-density lipoprotein. They act as a scavenger of free cholesterol and enhance the rate of clearance of cholesterol from the arteries. Serum high-density lipoprotein cholesterol levels and subsequent development of coronary artery disease in hypertension were also found to be related, but in hypertension through the effects of diet on plasma lipids.[13] The inverse proportion of the Framingham study.[2] Dietary factors and clinical events of coronary artery disease are linked together with high For these reasons, high density lipoprotein cholesterol is often referred to as good cholesterol. Henry P.D in 1981[8] showed that calcium channel blockers like nifedipine and nicardipine reduce atherosclerotic lesions in cholesterol fed rabbits without any significant effect on serum lipids.It has been reported that calcium channel blockers including nifedipine do not adversely affect lipid profile[7,14] Showed the beneficial effect of low dose felodipine on serum cholesterol of rabbits fed on atherogenic diet. The cholesterol reducing effect of felodipine, when administered early has not been explained

satisfactorily. Increased uptake and degradation of low density lipoprotein by skin fibroblasts, aortic endothelial cells, smooth muscle cell, induction of denovo synthesis of apoproteins and inhibition of cholesterol synthesis and reduction of cholesterol ester accumulation in smooth muscle cells are thought to be the possible mechanisms. Many studies have demonstrated that arterial compliance is improved by antihypertensive drugs that induce vasodilation in the large peripheral arteries, e.g. calcium antagonists, angiotension converting enzyme inhibitors and certain beta adrenoreceptor blockers. Amlodipine increased arterial compliance and dilated the brachial artery at prevailing and isobaric pressure. The active increase in arterial compliance with amlodipine was 26% of pretreatment values, while passive pressure dependent was only 14%.[10] It has been shown experimentally that a reduced response of the arterial smooth muscle to endothelial vasodilators and an increased sensitivity to vasoconstrictor agents may be involved in the abnormal arterial reactivity seem in hypercholesterolemia. The presence of calcium and its role in plaque formation is not yet fully elucidated.[6] Over the past decade, investigators have demonstrated that CCB like agents may retard plaque formation. Recent studies in patients with coronary artery disease have demonstrated that nifedipine may impede or prevent the development of atherosclerosis plaques in humans as well.[15]

CONCLUSION

The present study shows that amlodipine plays a favourable role in the alteration of serum cholesterol profile. Further studies confirming these findings may open up new avenues for this novel group of drugs and pave way for their use in many appropriate situations for prevention of hypercholesterolemia.

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