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REVIEW ARTICLE

EFFECT OF NICARDIPINE ON FASTING PLASMA LIPIDS AND APOLIPOPROTEINS IN MALE NEW ZEALAND WHITE RABBITS

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The effect of nicardipine on fasting plasma lipid profiles was studied in rabbits given a 2% cholesterol diet. Twenty four New Zealand White rabbits (2.2 - 2.8 kg) were divided into 3 groups. Group 1 (control) was fed a normal diet, group II (HC) was fed a 2% cholesterol diet and group III (HC+NICA) was fed a 2% cholesterol diet with nicardipine treatment (0.5mg kg^{-1} body weight twice daily intramuscularly for 10 weeks). The following parameters which included fasting plasma total cholesterol, triglycerides, HDL cholesterol and apolipoprotein A and B were measured before and after 10 weeks of study. In the present study we observed that a 2% cholesterol diet caused a significant increase in plasma total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides. However, the increase in total cholesterol and LDL cholesterol were not prevented by treatment with nicardipine. Nicardipine appeared to cause further increase in HDL cholesterol and prevented further rise in plasma triglycerides after 10 weeks of treatment.

***Key words**: nicardipine, lipid profile, cholesterol-rich diet, New Zealand White rabbits.*

Introduction

Hypercholesterolemia is a known major risk factor in the development of atherosclerosis (1-3). It can result from endogenous causes or from exogenous dietary source. Dietary hypercholesterolemia may result from high cholesterol intake or the increased intake of saturated fatty acids. Hypercholesterolemia, regardless of cause, influences the development of atherosclerosis. The incidence of coronary heart disease (CHD) remains high despite blood pressure being controlled in hypertensive patients (4-5). There is a possibility that the effects of antihypertensive drugs on lipid profiles may be offsetting the beneficial effects of blood pressure reduction in patients with CHD (4-5). Nicardipine is an intermediate acting calcium channel blocker of dihydropyridine subgroup. It blocks the influx of calcium into the smooth muscles and cardiac muscles via the voltage dependent calcium channel of predominantly of L subtype. This drug is being used to treat hypertension. The antihypertensive effect of this drug is mediated through it vasodilating properties. This study examined the effect of nicardipine (supplied by UNAMM Coperation Sdn Bhd Malaysia), on fasting serum lipid and apolipoproteins.

Materials and methods

Animals

Twenty four male rabbits of *Oryctologus cuniculus* species weighing 2.2-2.8 kg were housed individually and assigned at random into three groups. Group 1 (control) was fed a normal diet. Group II was fed daily 100 g of 2% cholesterol diet without nicardipine treatment. Group III was fed daily 100 g of 2% cholesterol diet with nicardipine treatment (0.5mg kg^{-1} body weight twice daily intramuscularly for 10 weeks).

Determination of plasma lipids and apolipoproteins

Fasting plasma lipids and apolipoproteins were measured before and after 10 weeks of study. Food was withdrawn for 12 hours overnight before blood samples were taken. Ten ml of blood was extracted from the central ear artery. Plasma total cholesterol, HDL cholesterol and triglycerides were analysed by enzymatic methods using kits (Boehringer Mannheim). For HDL cholesterol determination, selective chemical precipitation was employed.

The addition of phosphotungstic acid and magnesium ions to a sample aliquot led to the precipitation of VLDL, LDL and chylomicrons and separated HDL cholesterol which were contained in the supernatant. The supernatant was separated and HDL cholesterol measured using enzymatic method as for total cholesterol. The LDL cholesterol was indirectly determined using Friedewald formula. The serum apolipoproteins A and B were measured using kit from Boehringer Mannheim.

Statistical analysis

Results are expressed as mean with S.E.M. Statistical analysis was performed using student's t test. Differences were considered statistically significant when $p<0.05$.

Results

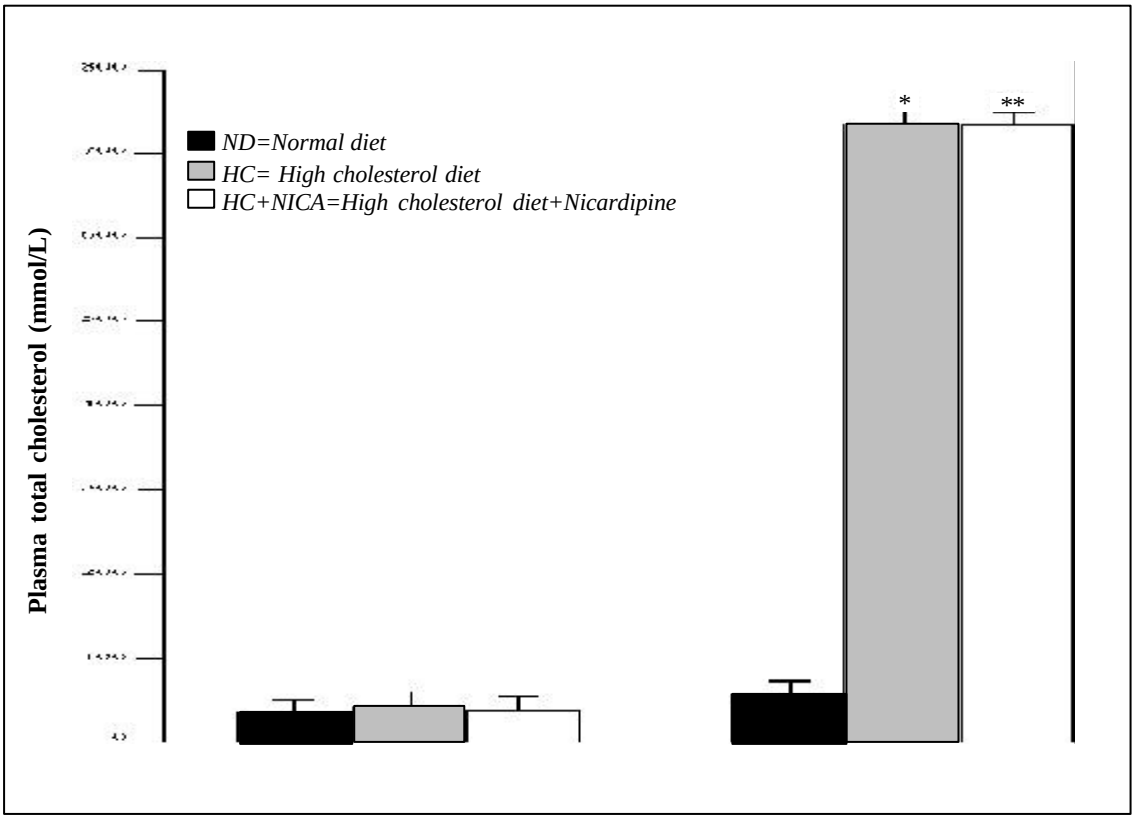
The body weight of the rabbits in each group increased at the end of the study (the body weight ranged between 2.31-2.39 kg before the study to 2.46-2.5 kg after the study). However, there was no difference in weight gained between the groups.

Effect of nicardipine on plasma total cholesterol.

There was no significant difference in fasting plasma cholesterol among the three groups at the start of the experiment. The plasma cholesterol concentration increased significantly ($p<0.05$) at the end of 10 weeks in the group given high cholesterol (atherogenic diet) diet with and without nicardipine treatment compared to their respective baseline levels (0 week).

However, there was no significant difference in the fasting plasma total cholesterol between the group given cholesterol diet alone and the group given cholesterol diet with nicardipine treatment (Fig. 1).

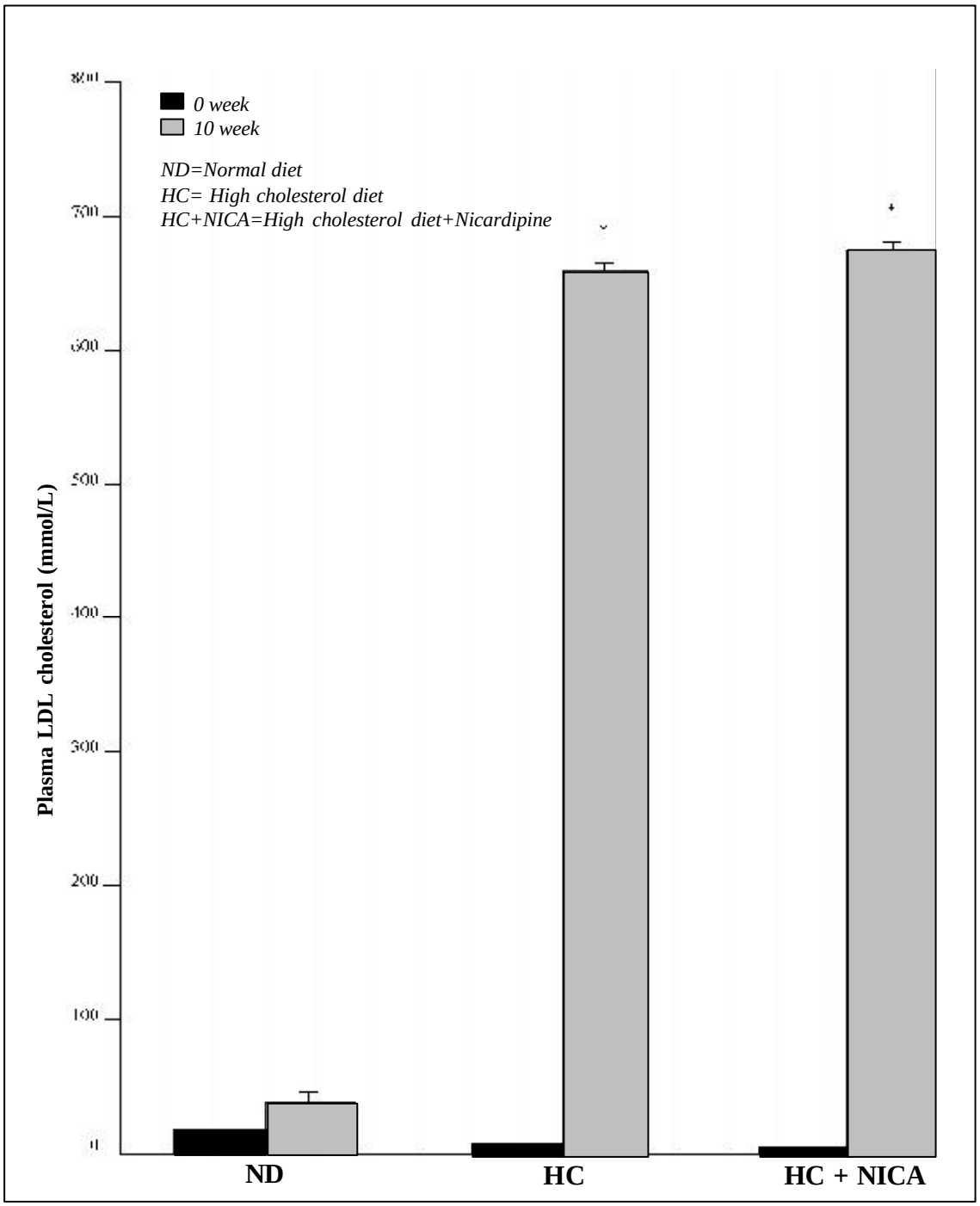
*Fig. 1: Changes in plasma cholesterol with atherogenic diet and nicardipine treatment.*p<0.05,**p<0.02 compared to respective values at 0 week*



Effect of nicardipine on plasma LDL cholesterol.

There was no significant difference in fasting plasma LDL cholesterol among the three groups at the start of the experiment. The plasma LDL cholesterol concentration increased significantly ($p<0.01$) at the end of 10 weeks in the group given high cholesterol diet with and without nicardipine treatment compared to their respective baseline levels (0 week). However, there was no significant difference in the fasting plasma LDL cholesterol between the group given cholesterol diet alone and the group given cholesterol diet with nicardipine treatment (Fig. 2).

*Fig. 2: Changes in plasma LDL cholesterol with atherogenic diet and nicardipine treatment.*p<0.01compared to respective values at 0 week*

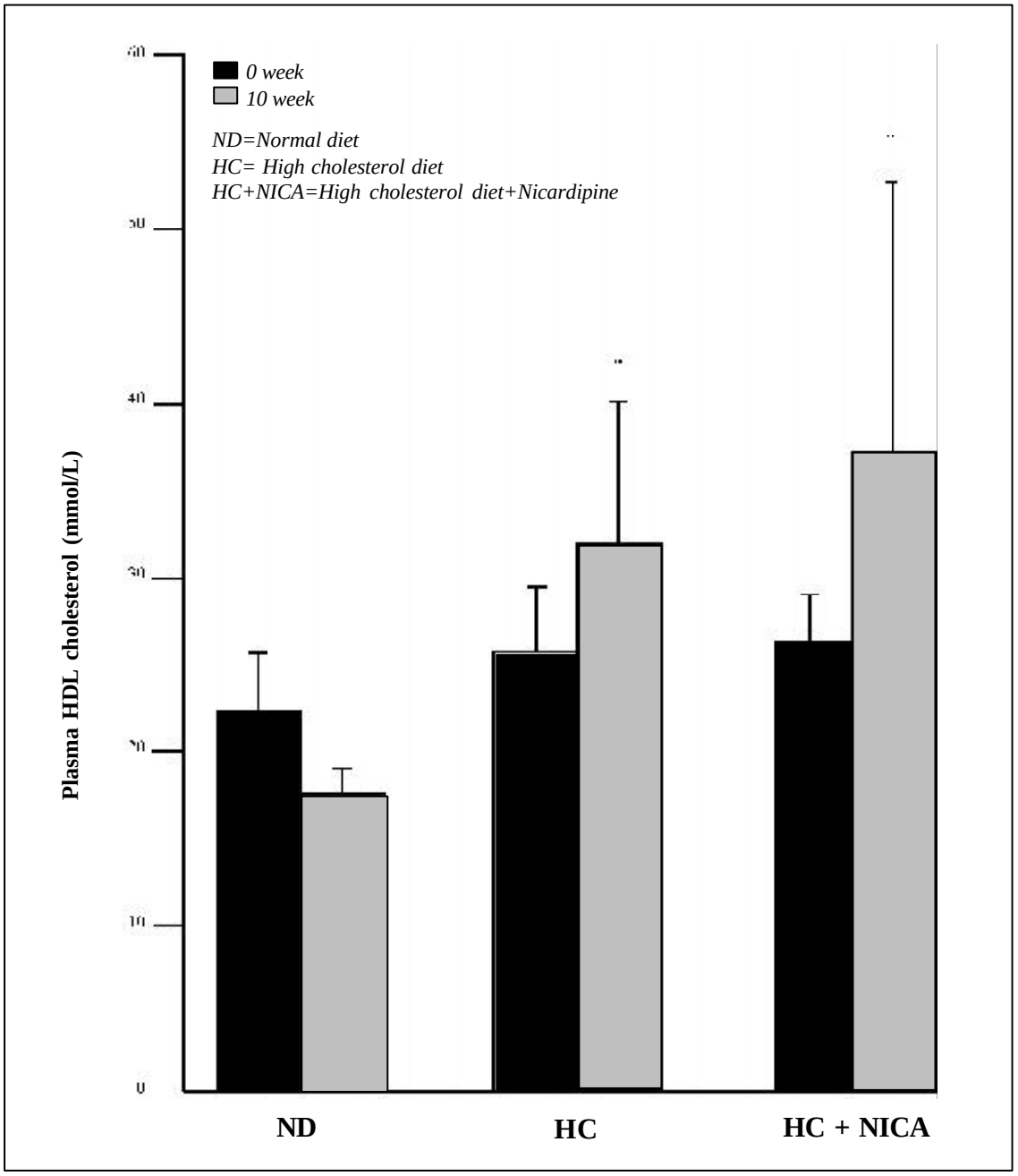


Effect of nicardipine on plasma HDL cholesterol

There was no significant difference in fasting plasma HDL cholesterol among the three groups at the start of the experiment. The plasma HDL cholesterol concentration increased significantly ($p<0.05$) at the end of 10 weeks in the group given high cholesterol diet with and without nicardipine treatment compared to their respective baseline levels (0 week).

However, there was no significant difference in the fasting plasma HDL cholesterol between the group given cholesterol diet alone and the group given cholesterol diet with nicardipine treatment (Fig. 3).

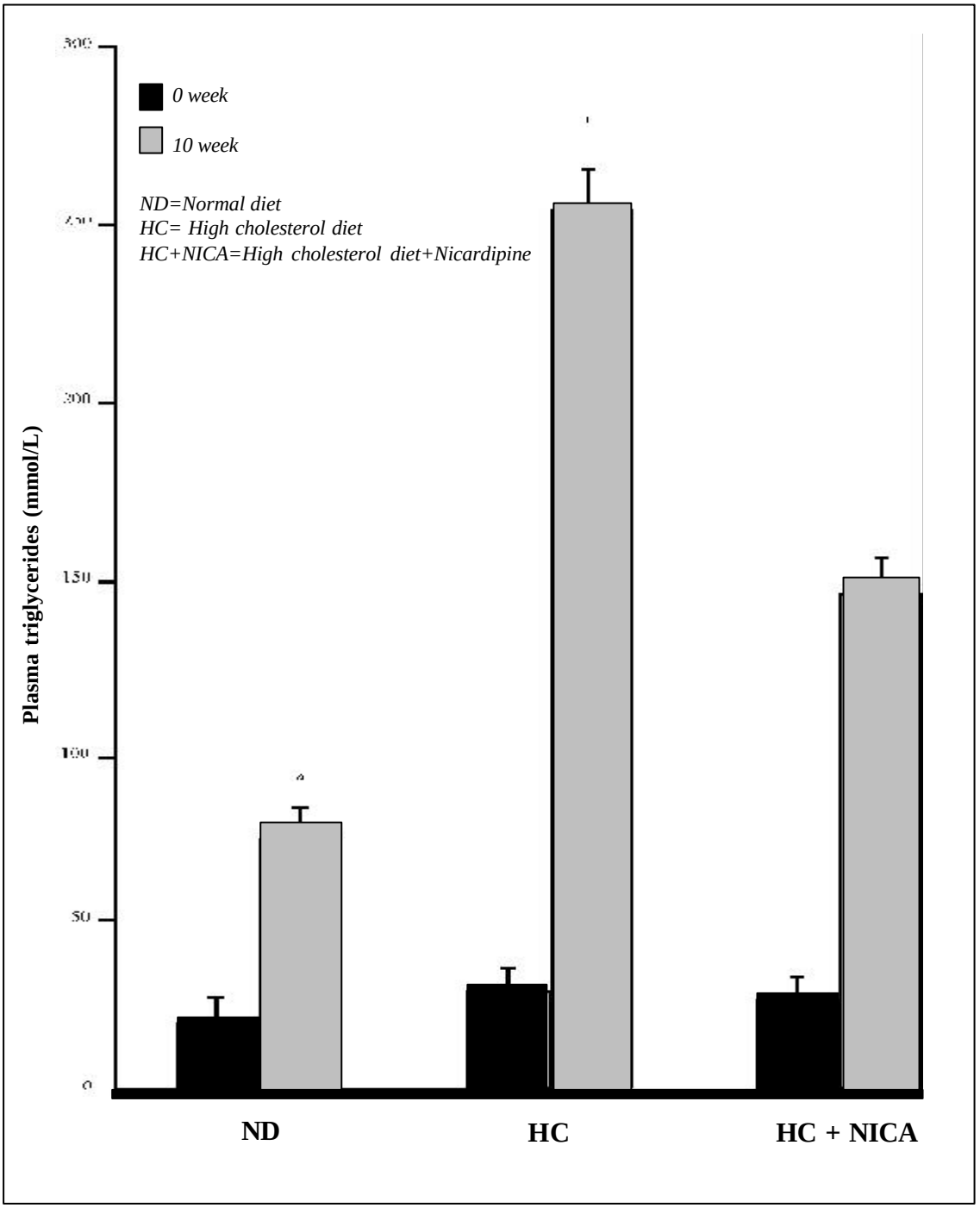
*Fig. 3: Changes in plasma HDL cholesterol with atherogenic diet and nicardipine treatment.*p<0.05 compared to respective values at 0 week*



Effect of nicardipine on plasma triglycerides

There was no significant difference in fasting plasma triglycerides among the three groups at the start of the experiment. The plasma triglycerides concentration increased significantly ($p<0.05$) at the end of 10 weeks in the group given high cholesterol diet with and without nicardipine treatment compared to their respective baseline levels (0 week). However the increase in the fasting plasma triglycerides in the nicardipine group was significantly less compared to the group without nicardipine treatment (Fig. 4).

*Fig. 4: Changes in plasma triglycerides with atherogenic diet and nicardipine treatment.*p <0.05 compared to respective values at 0 week*



Effect of nicardipine on plasma apolipoproteins A and B

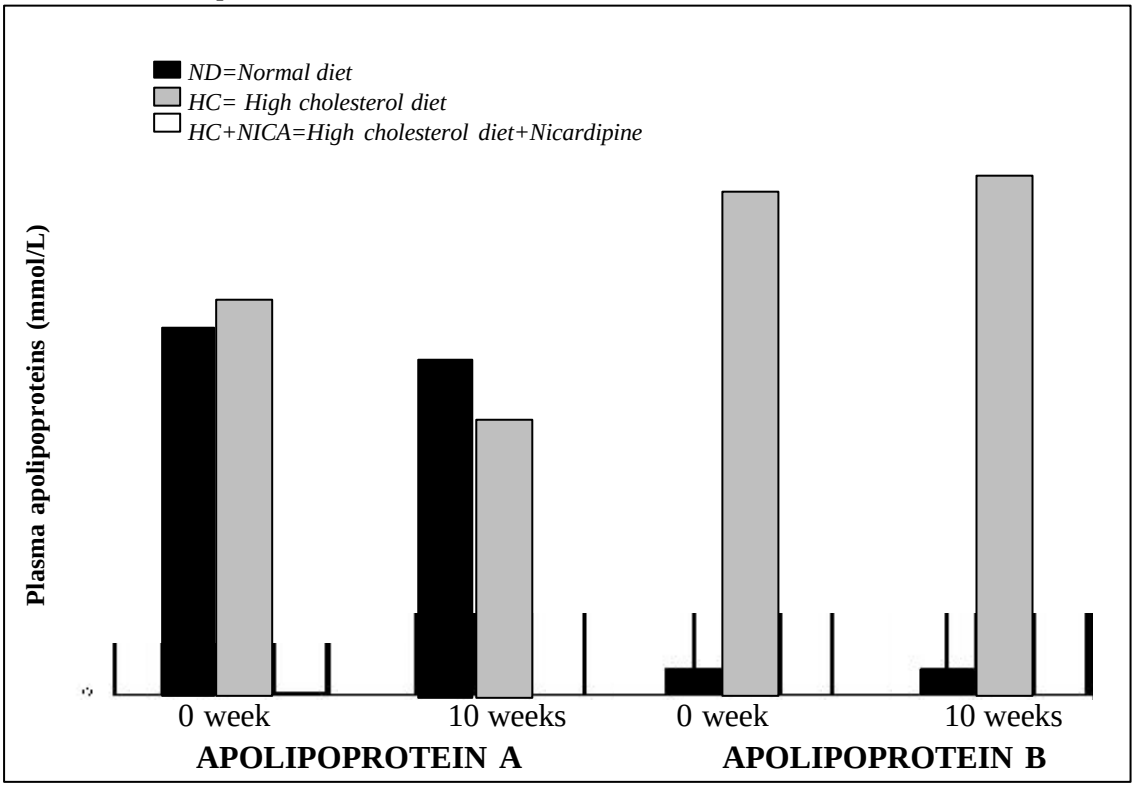
There was no significant difference in the fasting plasma apolipoprotein A and apolipoprotein B at the start of the experiment and at the end of 10 weeks of study among the three groups (Fig.5).

Discussion

Our earlier work has shown that a 2% cholesterol diet fed to a group of rabbits produced hypercholesterolemia (1). The rabbit model used in the present study was identical to the one used previously (1).

In the present study we observed that a 2 % cholesterol diet caused an increased in level of plasma total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides at the end of 10 weeks of study. However the increase in total cholesterol and LDL cholesterol were not prevented by treatment with nicardipine. Nicardipine appeared to cause further increase in HDL cholesterol but prevented further rise in plasma triglycerides after 10 weeks of treatment. This finding suggests that nicardipine only improves plasma HDL cholesterol and triglycerides in rabbits fed high cholesterol diet. The antiatherogenic effect of nicardipine that was observed in our previous studies (6,7) was unlikely to be due to changes in plasma lipid profiles.

Fig. 5: Changes in plasma apolipoprotein A and apolipoprotein B with atherogenic diet and nicardipine treatment



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