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Original Research Article

Status of Small Dense LDL in Cardiovascular Disease Subjects Taking Drug Therapy

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ABSTRACT

Increased plasma LDL-cholesterol (LDL-C) level is one of the most important risk factors for coronary artery disease. The LDL subfraction i.e. small dense LDL is more atherogenic form of the LDL and is observed as an important risk factor for coronary heart disease. Conventional treatment of atherogenic lipid profile aims at reducing total cholesterol, LDL cholesterol or increasing HDL cholesterol by using different treatment modalities available. In this study we aimed to compare the status of lipid profile and small dense LDL in cardiovascular disease subjects who were not taking any drug therapy before admission in hospital and those who were under the treatment. The study comprised of total 70 diagnosed subjects of coronary heart disease admitted in the ICU of J.A. Hospital out of which 30 subjects were included in group I who were not taking any drug therapy before admission in ICU and group II included 40 subjects who were under drug treatment. sdLDL- C levels did not show any significant difference between the two groups in spite of the drugs being given to the group II subjects. This result suggests that drugs therapy may be associated with a decrease in total LDL-particle concentration and other lipid parameters but not the proportion of small dense LDL-C.

Key Words: sdLDL-c, LDL, Cardiovascular disease

INTRODUCTION

Increased plasma LDL-cholesterol (LDL-C) level is one of the most important risk factors for coronary artery disease (CAD). [(1,2)] The increase in cholesterol and triglycerides is due to an increase in apolipoprotein B-containing lipoproteins, that is, very low density (VLDL) and low density lipoproteins (LDL). Thus, it is logical that LDL cholesterol remains the primary therapeutic target for coronary heart disease (CHD) prevention. It is the main cholesterol carrying lipoprotein in the circulation. LDL was originally thought to be monodisperse, i.e. composed of a distribution of particles which are heterogeneous and vary according to the size, the density and the composition of the fat they contain. In particular, small dense LDL (sdLDL) has been demonstrated to be a risk factor for the development of CVD. These small dense LDL particles appear in individuals who are hypertriglyceridemic and have a low concentration of HDL

cholesterol. Elevated LDL cholesterol, TGs and reduced HDL may be present in different individuals in varying combinations. The picture is complicated by the presence of small dense LDL. Moreover the patients with different LDL subfractions respond differently to different therapy. [3] The small, dense LDL particles cross very easily to the arterial endothelium and form complexes with the proteoglycans of the media, which undergo oxidation in their turn, thus increasing their atherogenic properties. It is believed that the creation of small, dense LDL is facilitated by an increase in triglycerides. [4] Conventional treatment of atherogenic lipid profile aims at reducing total cholesterol, LDL cholesterol or increasing HDL cholesterol by using different treatment modalities available. Several drug therapies are used to treat hyperlipidemia. [5] Certain class of drugs potentially lower all LDL subclasses (large, medium, and small particles); therefore, the net effect on LDL particle size is often null or, at most,only moderate. [6] Although statins clearly decrease total LDL particle concentration, it is a matter of debate whether statins reduce sdLDL predominantly. [7,8] Therefore we aimed our study to compare the status of lipid profile and small dense LDL in cardiovascular disease subjects who were not taking any drug therapy before admission in hospital and those who were under the treatment.

MATERIALS AND METHODS

The present study was conducted at department of Biochemistry and medicine department of J.A. Group of Hospitals, G.R. Medical College, Gwalior. The study comprised of total 70 diagnosed subjects of coronary heart disease admitted in the ICU of J.A. Hospital out of which 30 subjects were included in group I who were not taking any drug therapy before admission in ICU and group II included 40 subjects who were under drug treatment.

Inclusion criteria: subjects who were diagnosed with CHD and had symptoms like restlessness, chest pain and high blood pressure.

Exclusion criteria: subjects with any other disease except CHD were excluded from the study.

5ml of blood sample was obtained from each subject after overnight fasting in all aseptic precautions for the analysis of biochemical parameters. ECG, Hb%, total and differential leucocyte count, height and weight were recorded at the time of admission.

Blood sugar and lipid profile was estimated by standard biochemical Kits (Erba) using BS 400 fully automated analyser (Mindray). Small dense LDL was calculated by using the regression equation by Srisawasdi et.al. [9] This study was approved by institutional ethical committee & written consent was also obtained from the patients prior to study.

Statistical Analysis

Student's t -test was used to compare biochemical parameters between the groups. Pearson's correlation was done to determine the relation of small dense LDL and other risk variables. All analysis was done using Windows based SPSS statistical package (Version 16.0).

RESULTS

In CVD subjects who were under drug treatment and the subjects who were not taking any drugs before admission to the hospital, overall status of the physiological parameters including age, height, weight, BMI (kg/m^2) and hemoglobin showed no significant difference whereas systolic and diastolic blood pressure was significantly higher ($p < .001$) in group (I) compared to the controls (II) (TABLE 1).

TABLE 1: Characteristics of the subjects. (*p < .001)**

GROUPS		AGE	Ht.	Wt.	BMI	Hb%	SBP	DBP
GROUP I (without treatment) (n=30)	Mean ± S.D	54.45 ± 9.467	1.695 ± .0312	63.85 ± 5.132	22.237 ± 1.874	13.397 ± 1.111	165.5 ± 24.083	100 ± 21.878
GROUP II (on drug therapy) (n=40)	Mean ± S.D	52.850 ± 7.679	1.693 ± .0371	62.55 ± 4.395	21.850 ± 1.797	13.265 ± 1.127	119.5 ± 8.256***	78.5 ± 7.451***

There is significant decrease in total cholesterol (p<.001), triglycerides (p<.01), LDL-C (p<.05) in subjects of group II as compared to group I subjects except HDL which increased significantly (p <.05) whereas small dense LDL showed no significant change in group II subjects who were on drug therapy (p=NS) (TABLE -2).

TABLE 2: ***significant (p<.001) **significant (p<.01)*significant (p<.05) ^{NS} Non significant

GROUPS		BS	TC	TG	VLDL-C	HDL-C	LDL-C	sdLDL-C
GROUP I Without Treatment (n=30)	Mean ± S.D	82.44 ± 7.90	291.23 ± 23.41	186.33 ± 31.07	37.27 ± 6.21	40.80 ± 6.97	190.16 ± 45.89	57.33 ± 18.24
GROUP II With Treatment (n=40)	Mean ± S.D	83.91 ± 10.50^{NS}	218.93 ± 16.51***	205.49 ± 46.13**	41.10 ± 9.22**	41.96 ± 7.23*	160.33 ± 51.86*	57.16 ± 21.47^{NS}

DISCUSSION

Predominance of sd-LDL-C is a major component of an atherogenic lipoprotein phenotype, and a source of increased risk for coronary heart disease. Relative risk of all lipoproteins in CVD has been extensively studied and the principle target for cardiovascular preventive strategies has been the low density lipoprotein cholesterol. [10,11] In our study on comparing the lipid parameters between the two groups, we found that the lipid levels were close to normal range in the subjects who were under the treatment except small dense LDL. sdLDL- C levels did not show any significant difference between the two groups in spite of the drugs being given to the group II subjects. These results were similar to the findings of. [12,13] Conventional treatment of the atherogenic lipid profile aims at reducing the total cholesterol levels, LDL –C levels or increasing HDL-C by using different treatment modalities available and some lifestyle modifications. Drug therapy decreases intracellular cholesterol, increase LDL receptors and accelerate removal of LDL-C and triglyceride rich lipoprotein. [14] The most important and widely used drugs for the treatment of hypercholesterolemia are statins. They reduce the cholesterol level by inhibiting HMG-CoA reductase enzymatic activity, the rate limiting enzyme in biosynthetic pathway of cholesterol. These drugs decrease intracellular cholesterol, increase LDL receptors and accelerate removal of LDL-C and TGs-rich lipoprotein and constitute the first line of treatment for reducing LDL-C. Though statins are superior to all other medications for reducing LDL-C concentration but their effect on sd LDL-C is variable. [15,16]

One possible mechanism for lowering of LDL-C by drug therapy but not sdLDL-C is that upregulation of LDL receptor activity by statins decreases large, buoyant LDL more than small, dense LDL, because statins increase LDL receptor activity and large, buoyant LDL is a better ligand for the LDL receptor than is small, dense LDL. This result suggests that drugs therapy may be associated with a decrease in total LDL-particle concentration and other

lipid parameters but not the proportion of small dense LDL-C. [17]

CONCLUSION

It is therefore concluded that sd-LDL-C is a major component of an atherogenic lipoprotein phenotype, and a source of increased risk for cardiovascular disease. Drug therapy may decrease the concentration of total LDL but may not show effect on LDL subfractions i.e. small and dense LDL. It is suggested that the therapeutic inflection of sd- LDL often require the combination of different treatment of drugs, lifestyle modification and dietary intake, which may constitute both primary and secondary prevention of CVD. In addition, individualized treatment is required for proper assessment of various risk factors that promotes CVD, particularly sd-LDL.

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