Characteristics of Serum Lipid and Lipoprotein Patterns in Patients with Coronary Sclerosis and with the Slightest Hyperlipidemia*

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It is well established that hyperlipidemia is intimately related to the pathogenesis of atherosclerosis.

However, in daily practice we often observe patients with coronary sclerosis and without any such marked hyperlipidemia as that seen in American and European countries.

From this viewpoint, we examined serum lipids and lipoprotein patterns of patients with coronary sclerosis but without marked hypercholesterolemia. We also followed the changes in phenotype of hyperlipoproteinemia in the course of hyperlipidemia.

SUBJECTS AND METHODS

We chose only male patients having less than 300 mg/100 ml of serum total cholesterol concentration. Subjects with secondary hyperlipidemia were excluded. They were from 35 to 68 years old.

We make a diagnosis of coronary sclerosis in accordance with the clinical diagnostic criteria of coronary sclerosis established by the special study group of the Educational Ministry in 1960.

Namely, patients having old myocardial infarction were regarded as undoubted cases with coronary sclerosis (MI group, 27 cases, mean age 54 yr.). Patients having typical anginal attack and ischemic changes in ECG were taken as relatively certain cases with coronary sclerosis (CS group, 30 cases, mean age 51 yr.). Healthy subjects having no such history and no changes in ECG served as the control group (30 cases, mean age 50 yr.).

All samples were obtained in the 14-hour fasting state.

Total cholesterol (TC) was determined by the modified Zak-Henly's method. Digitonin precipitable cholesterol was measured as free cholesterol (FC). Serum triglyceride (TG) was determined by Fletcher's method. Lipid-phosphorus (P) was determined by the modification of Chen et al. (total phospholipid = lipid-P×25). Total lipids (TL) were calculated as TC + 0.73EC + TPL + TG. Free fatty acids (FFA) were measured by Dole's titration method. Lipoproteins were separated by the disc electrophoresis on polyacrylamide gel (Canalco, QDL kit) and by agarose-agar gel electrophoresis.

RESULTS

As shown in Fig.1, total cholesterol was significantly higher in the MI group than in the CS and the control group, but no difference was observed between the CS and the control group.

Nevertheless, FC, TG, TPL and TL increased stepwise in the control, the CS and the MI group in this order. Comparing with the control group, FC, TPL and FFA were significantly higher in the MI and the CS group. Except TC and EC, no significant differences were observed in other lipid fractions between the MI and the CS group.

Key Words:
Coronary sclerosis
Lipid and lipoprotein fractions
Extra pre-β lipoprotein

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Fig. 1. Concentrations of major fractions of serum lipids in the control, coronary sclerosis (CS) and myocardial infarction (MI) group (Mean ± SE).

Fig. 2. Percent distribution of major lipoprotein fractions determined by densitometry on disc electrophoresis and their ratios. (Mean ± SE).

The TC/TPL ratio was significantly higher in the CS group than in the control one.

As for lipoprotein fractions (Fig. 2), the percentage of pre-β lipoprotein and the ratio of β/α and pre-β + β/α increased stepwise in the control, the CS and the MI group in this order. The percentage of β lipoprotein was significantly higher in the CS and the MI group than in the control one. In the CS and the MI group, the percentage of α lipoprotein was significantly lower than that in the control group.

Taking together with the results of serum lipids, these findings suggest that the pathological alterations in lipid metabolism in CS and MI are associated with increased uptake of pre-β lipoprotein and decreased clearance of β lipoprotein.

TABLE I  FREQUENCY OF HYPERLIPOPROTEINEMIA CLASSIFIED BY WHO PROPOSAL IN THE CONTROL, CORONARY SCLEROSIS (CS) AND MYOCARDIAL INFARCTION (MI) GROUP

<table>
<thead>
<tr>
<th>Type</th>
<th>normal</th>
<th>IIa</th>
<th>IIb</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>n=30</td>
<td>17 (57%)</td>
<td>4 (13%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CS</td>
<td>n=30</td>
<td>16 (54%)</td>
<td>4 (13%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>MI</td>
<td>n=27</td>
<td>10 (37%)</td>
<td>6 (18%)</td>
<td>4 (18%)</td>
<td>0</td>
</tr>
</tbody>
</table>

TABLE II  FREQUENCY OF SO-CALLED EXTRA PRE-B LIPOPROTEIN ON DISC ELECTROPHORESIS IN THE CONTROL, CORONARY SCLEROSIS (CS) AND MYOCARDIAL INFARCTION (MI) GROUP

| Type | | |
|------|-----|-----|-----|-----|-----|
| Control | n=30 | 6/130 (20%) |
| CS | n=16 | 16/130 (53%) |
| MI | n=14 | 27/127 (52%) |

Lipid fractions, these results of lipoprotein fractions were intriguing.

The frequency of phenotype of hyperlipoproteinemia classified by WHO proposal was shown in Table I. To classify hyperlipoproteinemia into the phenotypes, we regarded 220 mg/100 ml for total cholesterol and 120 mg/100 ml for triglycerides as the upper limits of normal values, respectively. As shown in Table I, Type IIb was tended to increase in the MI group, but no difference in the frequency of Type IIb was observed between the control and the CS group.

So-called extra pre-B lipoprotein on disc electrophoresis was observed more frequently in the CS and MI group than in the control group (Table II).

As for the changes in the phenotypes of lipoprotein pattern with time, Type IIa and IV did not change into other types but Type IIb changed occasionally into Type IIa.

These results suggested that even slight changes in serum lipid and lipoprotein patterns might be related to atherogeneity.

**Conclusion**

1. Serum lipid and lipoprotein patterns of subjects with/without coronary sclerosis and having less than 300 mg/100 ml of serum total cholesterol were analyzed. Subjects with coronary sclerosis were classified into 2 groups, myocardial infarction (MI) group and coronary sclerosis (CS) group, in accordance with the criteria for the diagnosis of coronary sclerosis established by the special study group of the Educational Ministry in 1960.

2. While serum total cholesterol was higher in the MI group than in the other groups, there was no difference in total cholesterol concentration between the CS group and the control. However, the concentration of free cholesterol, triglycerides, total phospholipids and total lipids increased in the control, the CS and the MI group in this order.

3. The percent concentration of pre-B and B and the ratio of B/α and pre-B+β/α increased in the control, the CS and the MI group in this order. Type IIb hyperlipoproteinemia was observed more frequently in the MI group than in the control one. Type IIa and IV hyperlipoproteinemia did not change into any other phenotypes, but Type IIb changed occasionally into Type IIa.

4. So called extra pre-B lipoprotein was observed more frequently in the CS and MI groups than in the control one.

5. These results suggested that even slight changes in serum lipid and lipoprotein patterns might be related to atherogeneity.