SERUM LIPID AND APOLIPOPROTEIN PROFILES AFTER ONSET OF ACUTE MYOCARDIAL INFARCTION

JUN SASAKI, M.D., TOMOKI KAWANO, M.D., YASUSHI SASAKI, M.D.
YASUYUKI ISHIHARA, M.D.*, TEIZO SATA, M.D.
AND KIKUO ARAKAWA, M.D.

The concentrations of lipids and apolipoproteins in serum following onset of acute myocardial infarction were measured periodically in eleven patients for 28 days.

Significant and sustained decrease in the concentration of HDL-cholesterol was observed by the seventh days post-infarction and remained low throughout the remainder of the study. The concentration of apo A-I and apo A-II assayed by electroimmunoassay was significantly low by 4th and 5th days post-infarction, remained low until day 10 and then began to increase but were not back to the initial values by 28 days post-infarction. Apo B, C-I, C-II, C-III, and E levels remained unchanged throughout the course.

The concentrations of total cholesterol, triglycerides tended to fall reaching the lowest levels on day 7 and 10, but were not significant. The concentration of serum phospholipids level tended to decrease and fall significantly by day 7 and 10. The concentration of the free fatty acids in the serum was elevated during the first 2 days post-infarction and was within the normal range throughout the remainder of the study.

ACUTE myocardial infarction is one of the most serious health problem in Western society and results in many metabolic changes. For instance, it has been reported that the concentration of total cholesterol (TC),¹⁻⁵ phospholipids (PL),⁴ LDL-cholesterol,^{5,6} apo B,⁵ and apo A-I,^{5,6} in serum fall significantly following acute myocardial infarction. At the same time, concentration of triglycerides (TG) increases,^{4,5} but others have failed to confirm this observation.⁶ No significant changes in concentration of HDL-cholesterol (HDL-C)^{2,5} in serum after onset of acute myocardial in-

farction were observed whereas in the recent report, HDL-C decreases significantly after myocardial infarction.⁶ Since little data is available on the apolipoprotein profile in serum after onset of acute myocardial infarction, the change in concentration of both the serum lipids and the serum apolipoproteins (i.e. apo A-I, A-II, B, C-I, C-II, C-III and E levels) after onset of acute myocardial infarction was determined.

SUBJECTS AND METHODS

Eleven patients (10 male, 1 female), aged 58 to 80 years were included in the present study (Table I). All had suffered the first attack of acute myocardial infarction within 12 hrs prior to admission to the coronary care unit of Fukuoka University Hospital and Ishihara

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Second Department of Internal Medicine, Fukuoka University Hospital, Fukuoka, Japan, *Ishihara Cardiovascular Clinic

Mailing address: Sasaki Jun, M.D., Second Department of Internal Medicine, Fukuoka University Hospital, 45-1, 7-chome, Nanakuma, Jyonan-ku, Fukuoka 814-01, Japan

TABLE I CLINICAL DATA OF 11 PATIENTS

Name	Age (sex)	Site of infarction	Maximum ESR	Maximum GOT	Maximum LDH	Maximum CPK	Maximum HBD
1. S.Y.	76 (M)	inferior	90	195	1297	125	625
2. K.T.	78 (M)	inferior	65	191	1139	127	430
3. F.N.	65 (M)	anterior	48	237	1790	107	762
4. M.J.	64 (M)	anterior	75	274	2219	129	831
5. A.S.	79 (F)	subendocardial	60	31	460	25	231
6. Y.K.	58 (M)	subendocardial	95	533	3580	105	1056
7. N.K.	72 (M)	anterior	89	159	1396	99	588
8. T.K.	69 (M)	anterior, inferior	55	123	1704	154	378
9. I.T.	72 (M)	anterior	62	317	2721	189	729
10. K.K.	54 (M)	anterior	64	214	1388	102	394
11. M.J.	80 (M)	anterior, posterior	27	286	2331	222	848

ESR = mm.; GOT = K.U.; LDH = W.U.; CPK = I.U.; HBD = U/ml

TABLE II SERUM LIPIDS AND APOLIPOPROTEINS CONCENTRATIONS ON THE FIRST DAY OF ACUTE MYOCARDIAL INFARCTION a)

	Normal b)	The first day of AMI	Significance
n	43	11	
Age	61 ± 10	70 ± 9	
TC (mg/dl)	197 ± 42	182 ± 27	NS
TG (mg/dl)	133 ± 57	139 ± 79	NS
HDL-C (mg/dl)	50 ± 13	41 ± 8	p < 0.05
Apo A-I (mg/dl)	127 ± 24	109 ± 18	p < 0.05
Apo A-II (mg/dl)	32 ± 6	31 ± 6	NS
Apo B (mg/dl)	116 ± 42	107 ± 31	NS
Apo C-I (U) c)	108 ± 28	106 ± 29	NS
Apo C-II (mg/dl)	4.0 ± 1.7	3.5 ± 1.6	NS
Apo C-III (mg/dl)	11.7 ± 5.4	9.4 ± 3.2	NS
Apo E (U) c)	101 ± 32	101 ± 23	NS

a) Values are mean ± SD.

b) Normal control groups consist of 26 men and 17 women who had no coronary artery diseases based on the coronary arteriogram.

c) Calculated based on the apo C-I and E content in the pooled serum of healthy men as 100 units.

Cardiovascular Clinic. No evidence of reinfarction during the study was observed. Diagnosis was made based on the clinical history, increased levels of serum enzymes (GOT, CPK, HBD, LDH) and characteristic serial electrocardiograms. The blood samples were drawn every day for 5 days and then on 7, 10, 14, 21 and 28th days post-infarction. All the patients were maintained on a restricted calorie diet program: day 1, 300 Cal/day (carbohydrate 100%); days 2–7, 1200

Cal/day (protein 22%, fat 31%, carbohydrate 47%); days 8–28, 1800 Cal/day (protein 13%, fat 30%, carbohydrate 56%). No patient was taking heparin, steroids, or other drugs known to affect lipids metabolism. No severe complications were observed. Blood was drawn via venous infusion line or venipuncture after at least 8 hrs fast. Samples were centrifuged at 3000 rpm for 15 minutes, the serum stored at 4°C and all analyses were carried out within 48 hrs.

Fig.1. Concentrations of total cholesterol (TC), triglycerides (TG), phospholipids (PL) and free fatty acids (FFA) in serum during the course of an acute myocardial infarction. The values are expressed as mean $\pm$ SD. Significant differences (*: $p < 0.05$, **: $p < 0.02$) were obtained compared to the values on the day of onset. The range of FFA in normal adult serum was 0.17–0.59 mEq/L.

Cholesterol, triglycerides and phospholipids were quantitated enzymatically.^{7–9} HDL-C was determined by the heparin-MnCl₂ precipitation method.¹⁰ The coefficients of variation of duplicate determination were 2.8%, 3.0%, 2.6% for TC, TG and HDL-C respectively. Electro-immunoassays were used to measure apo A-I, A-II, B, C-II, C-III and E.¹¹ Radial immunodiffusion procedure was used to measure apo C-I.¹² The antiserum to apo A-I, A-II, B, C-I, C-II, C-III and E were monospecific as judged by double immunodiffusion against serum lipoproteins and other apolipoproteins.¹³ Statistical significance was evaluated using a two-tailed Student's *t* test.

RESULTS

The initial concentrations of serum lipids and

Fig.2. The concentrations of HDL-cholesterol (HDL-C) in serum during the course of acute myocardial infarction. The values are expressed as mean $\pm$ SD. Significant differences (**: $p < 0.02$, ***: $p < 0.001$) were calculated as compared to the initial values obtained on the day of onset.

Fig.3. The concentrations of apolipoproteins A-I, A-II and B in serum during the course of an acute myocardial infarction. The values are expressed as mean $\pm$ SD. Significant differences (*: $p < 0.05$, **: $p < 0.02$, ***: $p < 0.001$) were calculated as compared to the initial values measured on the day of onset.

apolipoproteins determined within the first day following onset of acute myocardial infarction for the 11 patients are tabulated in Table II. The concentrations of HDL-C and apo A-I in the serum from these 11 patients were significantly lower than obtained from normal adults.

Fig. 4. The concentrations of apolipoproteins C-I, C-II, C-III and E in serum during the course of acute myocardial infarction. The values were expressed as mean $\pm$ SD.

The serum phospholipid levels tended to decrease and there was a significant fall by 13 and 12% on day 7 and 10, respectively. The serum TC levels tended to fall reaching the lowest value on day seven (182 ± 27 to 166 ± 36 mg/dl), but was not significant. The TC levels on admission ranged 150 to 230 mg/dl and a decrease in TC level was found in 9 patients following myocardial infarction. The TG levels fell following myocardial infarction, but was not significant (Fig. 1). The mean concentration of free fatty acids in the serum was higher than the normal ranged 0.17–0.57 mEq/L during the first 2 days period. In contrast the mean HDL-C levels were significantly low on admission (Table II), decreased to the lowest level by 7th days

post-infarction, and remained low throughout the study (Fig. 2). Likewise, the mean apo A-I concentration initially observed was significantly low, decreased to minimal value by day 7 and increased slightly through the remainder of the study. At 28 days post-infarction the apo A-I concentration was approximately 75% of normal. The initial mean apo A-II concentration was normal and then dropped significantly reaching the lowest level on the 10th days post-infarction. The apo A-II concentration had increased to about 80% of the normal adult concentration by 28 days post-infarction (Fig. 3). The mean concentrations of apolipoproteins B, C-I, C-II, C-III and E were not significantly different from controls on the day of admission, and did not significantly change throughout the study (Fig. 4).

DISCUSSION

The decreased concentration of TC and increased concentration of TG in the serum following acute myocardial infarction previously reported have not been confirmed in the present study. No consistent changes in HDL-C concentration after onset of acute myocardial infarction have been reported, but in this study a significant sustained decrease in the HDL-C was noted.

The reasons for the these discrepancies are not yet clear, however, the initial mean TC concentrations reported in previous studies^{1–5} are considerably higher (257 to 301 mg/dl) than normal. Dodds et al. reported that the largest post-infarction variations in lipids level have been observed in patients whose pre-infarct level was high, those with a low level showing little or no change? Furthermore, it is the younger patients with coronary artery disease who, in general, have high lipoprotein levels, while elderly tend towards the normal? Since patients studied in this study had normal TC level (mean, 182 mg/dl) on the day of myocardial infarction and the higher mean patients age of 70 yrs compared to reported age of 54 to 63 yrs, the normal TC level and relatively older patients group may contribute to small changes in TC concentrations observed in this study. In addition, as pointed out by Watson that the severity of myocardial damage correlates to the degree of fall in TC, relatively mild cases in this study may also contributed to the small changes in TC levels. Changes in TG levels after myocardial infarction have many possible explanations: basal TG level,

increased free fatty acids, diet, body weight, drugs and the severity of myocardial damage. Decreased TG level observed in this study may account for the normal TG levels on the first day and less severe myocardial infarction. We did not see increase in TG levels while free fatty acids level increased above normal limit. The serum HDL levels are influenced by variety of factors including sex, cigarette smoking, alcohol consumption and exercise.¹⁴ Since low HDL-C levels are significantly correlated to low physical activities in survivors of myocardial infarction,¹⁵ the sustained low levels of HDL-C may be in part result from low physical activity.

The apolipoproteins are known to regulate lipoprotein metabolism in the plasma. Significant decreases in the concentrations of apo A-I^{5,6} and apo B⁵ following onset of acute myocardial infarction have been reported. In this study, decreased concentrations of apo A-I and apo A-II in serum after myocardial infarction have been observed. However no significant changes in the concentrations of apolipoproteins B, C-I, C-II, C-III and E were observed. Although no statistical significance was found, the HDL-C and apo A-I ratio which was 0.366 ± 0.06 on admission increased to 0.438 ± 0.09 by 4th day and then decreased gradually to 0.337 ± 0.08 by 28th days post-infarction. These data indicate decreased HDL molecule as well as changes in composition following myocardial infarction. Avogaro et al. reported apo C changes following myocardial infarction estimated by urea polyacrylamide gel electrophoresis. They found increased apo C-II, C-III and C-III/C-II ratio and led to the speculation of impaired lipoprotein lipase activity and high TG levels after myocardial infarction.⁵ Recently Stubb et al. reported decreased HDL-C level and altered activation characteristics of lipoprotein lipase by patients serum with acute myocardial infarction, however, no significant changes in TG level was observed.⁶ In this study, C-III/C-II ratio tended to decrease from 1.23 ± 0.37 (the first day) reaching the lowest level of 0.91 ± 0.25 on 7th day, but was not significant. No apparent correlation was found between C-III/C-II ratio and serum TG levels following acute myocardial infarction.

The mechanism for the changes in lipoproteins after acute myocardial infarction remained unknown, but are either increased catabolism or impaired biosynthesis. Since similar changes have been reported in burn patients,¹⁶ change in permeability across

membrane may be contributed to these changes.

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