Variations in the Composition of Low- and High-Density Lipoproteins during the Acute Phase of Myocardial Infarction

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We analyzed correlations between apolipoprotein B (apo B), cholesterol and phospholipids (preponderant lipids) in low-density lipoproteins (LDL) as well as between apolipoprotein A1 (apo A1) and these same lipids in high-density lipoproteins (HDL), during the acute phase of myocardial infarction. In LDL, a very elevated and stable correlation (r) was observed between these parameters, and the coefficients of regression (b) did not differ significantly during the period studied. In HDL, there was a decrease in r and b values from day 1 to day 2, then an increase after day 2. We hypothesize that these disturbances in HDL composition may be due to a greater endocytosis of LDL at day 2, leading to intracellular increase in cholesterol and phospholipids. Part of these lipids could be taken up by HDL molecules, causing a transient overload.

Several studies relative to the acute phase of myocardial infarction (MI) have indicated changes in lipids and lipoproteins (1–4), particularly in low-density (LDL) and high-density lipoproteins (HDL).4 However, to our knowledge, no research has been carried out on possible disturbances in the composition of LDL and HDL during this same interval.

The purposes of the present study were (a) to determine concentrations of apolipoprotein B, cholesterol, and phospholipids (preponderant lipids) in LDL, as well as between apolipoprotein A1 (apo A1) and these same lipids in HDL, and (b) to analyze correlations between these constituents in each type of lipoprotein.

Materials and Methods

Blood was sampled from 22 patients (18 men, four women, 45 to 83 years of age) admitted to hospital for recent MI (less than 24 h after the first clinical signs). The treatment of these patients consisted of administration of six tablets of isoosorbide dinitrate (Risordan; Laboratoires Théraplix, 75640 Paris Cedex 13, France) per day and of calcium heparinate (Calciparine; Laboratoires Choyé, 75782 Paris Cedex 16, France) three times per day. Diabetic subjects and those treated with β-blocking substances were excluded from the study.

Samples from subjects who had fasted for at least 14 h were collected in tubes without anticoagulant on the first (day 1), second (day 2), fourth (day 4), and eighth (day 8) days of MI. After 30 min, the blood was centrifuged at 1500 × g for 15 min, and the sera were then stored at 4 °C. Ultracentrifuged fractions were isolated according to the method of Havel et al. (5) in a Beckman U50 ultracentrifuge with Ti 05 rotor. Cholesterol and phospholipids were assayed by enzymatic methods based on the Trinder reaction (6) (PAP enzymatic cholesterol, cat. no. G122-6, Biomérieux, Marcy l’Etoile, France; and phospholipids B test, Wako, Biolyon, France). Apo A1 and apo B were assayed by electromuodiffusion according to the method of Laurell (7), with use of Apofilm plates (Sèbia, Isay-les-Moulineaux, France).

Changes in variables in patients were analyzed by Student’s t-test for serial measurements. The normality of the different series of values was checked by using the test of Shapiro and Wilks. Regression-line equations were determined by the least-squares method, and comparison of the coefficients of regression was carried out by Student’s t-test after homogeneity of residual variances was checked (8).

Results

Values for LDL-cholesterol (Table 1) decreased significantly between day 1 and day 2 (P <0.001) but presented no appreciable variation after day 2. There was also a significant decrease of LDL-phospholipids (P <0.025) and LDL-apo B (P <0.001) between days 1 and 2.

A very elevated correlation was noted between LDL-cholesterol and apo B (Table 2). This correlation was quite stable (0.91 < r < 0.93), with a very high statistical significance (P <0.001). Moreover, the coefficients of regression (b) did not differ significantly during the period studied.

The same observations apply to the correlation between phospholipids and the apo B of LDL (Table 3): coefficients of correlation ranged between 0.83 and 0.90 (P <0.001), and b values between 0.15 and 0.18.

In contrast to LDL-cholesterol, HDL-cholesterol (Table 1) did not change significantly from day 1 to 2. Rather, it tended to increase slightly, with a decrease observed from day 2 to 8. The apo A1 concentration did not follow quite the same course as HDL-cholesterol, showing a progressive decrease from day 1 to 8 (P <0.03).

A significant correlation was noted between cholesterol and apo A1 (Table 4) during the period studied. However, from day 1 to 2 there was a decrease in r values, with a lowering in the degree of significance (P <0.001 at day 1, P <0.01 at day 2), followed by an increase in values at days 4 and 8. The coefficient of regression b decreased significantly from day 1 to 2, then increased after day 2.

If correlations between phospholipids and apo A1 are considered (Table 5), the same observations may be made: lowering of r values, and of their degree of significance, from day 1 to 2 (P <0.001 at day 1, P <0.05 at day 2), followed by an increase after day 2. There was also a significant decrease in the coefficient of regression b from day 1 to 2.

Discussion

Our variations in HDL and LDL lipoproteins generally agreed with those of previous studies. A drop in LDL-cholesterol has been noted by several authors (1, 3, 9, 10), Avogaro et al. (1), and Ryder et al. (3) found a slight decrease after day 2. The decrease noted in apo B also

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4 Nonstandard abbreviations: MI, myocardial infarction; HDL, LDL, high- and low-density lipoproteins; apo, apolipoprotein.

Received February 23, 1987; accepted October 22, 1987.
confirmed earlier findings (1, 9), and the decrease in HDL-cholesterol and apo A1 subsequent to infarction has also been found in different investigations (1-3, 11). However, to our knowledge, LDL-phospholipids have not been studied in this clinical context. If the correlations between cholesterol and apo B and phospholipids and apo B in LDL are considered, the very high statistical significance and the stable values for the coefficient of regression suggest a constant LDL composition with respect to the three constituents, despite a decline in these lipoproteins at day 2.

The same is not true for HDL. In the correlation between HDL-cholesterol (x) and apo A1 (y), the significant decrease in the coefficient of regression b at day 2 indicates a transient excess of cholesterol in HDL, whereas the degree of significance of r becomes lower. The same findings characterized the correlations between HDL-phospholipids (x) and apo A1. Thus, HDL presented a more unstable composition at day 2, precisely at the time that LDL declined.

If it is considered that the drop in LDL corresponds to increased endocytosis of these lipoproteins, there would be a transient increase in the intracellular concentration of phospholipids and cholesterol. A part of these lipids could then be taken up by HDL, which would suppose a change in equilibrium among these lipoproteins, which in fact represent a heterogeneous group of molecules, both in their apolipoprotein (A1, A2, C, E) and lipid (particularly nonesterified and esterified cholesterol) composition.

This brief preliminary study serves to call attention to the instability of the HDL equilibrium during the acute phase of MI. Further investigations relative to analysis of HDL subfractions should allow the specific nature of the lipoproteins involved in this disturbance to be determined.

References