Plasma Cephalins of Patients with Acute Myocardial Infarction

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The view is widely accepted that there is an association between atherosclerosis and the faulty metabolism of lipids. The lipid measurements thought to reflect such disturbance in lipid metabolism include cholesterol, cholesterol-phospholipid ratio, triglycerides, and lipoproteins. Perhaps the investigation of lipid metabolism in its relationship to atherosclerosis may properly include the phospholipids and, in particular, the cephalins since, among other things, they appear to be involved in the clotting mechanism. This mechanism in turn is thought to bear an important relationship to the overall problem of atherosclerosis.

We previously reported that small amounts of cephalins were detected regularly in the plasma of normal individuals and that the values were two to three times as high in patients with chronic coronary heart disease as in normal subjects. Martinetti and associates found that concentrations of the phosphatidyl ethanolamine in the plasma of four normal persons were 2.6% of the total phospholipids and in 13 patients with coronary heart disease (presumably acute) 4.2%. Our own figures are 3.0% for normal subjects and 5.5% for patients with chronic coronary heart disease. Although the methods used were different, the results, at least in the normal subjects, are in agreement. Furthermore, Heyrovský and Heyrovská demonstrated a relative decrease in lecithin and an increase in the cephalin serum fraction in clinical atherosclerosis. In collaboration with Reinš, one of these authors showed that similar changes exist in experimental atherosclerosis.

The present report deals with measurements of the cephalins, phosphatidyl ethanolamine, and phosphatidyl serine in the plasma after an acute attack of myocardial infarction.

Methods

The 65 patients included in this study were all under observation on the medical service of the New England Medical Center Hospitals. Fifty-six were admitted to the hospital within 24 hours of the recognizable onset of the acute myocardial infarction, and nine entered the hospital on the second day after the incident. The blood for the determinations of the lipids was drawn immediately after the patients had been admitted to the hospital and subsequently in mornings, after at least a 12-hour fast. The determination of the cephalins was carried out according to the method of Axelrod and associates. Phospholipids were determined by the method of Fiske and Subbarow, and cholesterol, by the method of Schoenheimer and Sperry. The determinations of cephalins were repeated daily for three days and then about every 2 or 3 days, until 2 weeks had passed.

Results

The values for phosphatidyl ethanolamine on the first 3 days immediately after the myocardial infarction and 1, 2, and 4 weeks

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thereafter, are shown in figure 1. On the first day after infarction phosphatidyl ethanolamine values in 56 patients ranged from 14.24 mg% to 54.1 mg%. The value of 54.1 mg% is the highest that we have found in our studies. It was noted in a 64-year-old patient shortly after the infarction occurred and only a few hours before she died. The next highest values were found in a group of 10 patients, who had levels of phosphatidyl ethanolamine ranging between 35 mg% and 40 mg%. The remaining 45 patients showed values from 14.26 mg% to 34.2 mg%. The average in all 56 cases was 29.7 mg%. In comparison, as noted in figure 1, the average value in 70 patients with chronic coronary heart disease was 18.0 mg% (range 8.88 mg% to 38.6 mg%) and in 70 normal individuals was 6.6 mg% (range 3.5 mg% to 9.49 mg%).

It appears then that in the first 24 hours after an acute myocardial infarction phosphatidyl ethanolamine is 50% to 100% higher than it is in patients with chronic coronary heart disease. On the second and third days after infarction phosphatidyl ethanolamine values usually declined some, although in six of the observed patients they rose. On the second day the range was from 16.06 mg% to 36.54 mg%, with an average of 25.3 mg% in 59 patients (six had died within 24 hours), and on the third day from 14.5 mg% to 34.59 mg%, with an average of 23.6 mg% in 57 patients (two more had succumbed). The decline continued slowly. By the end of the first week after infarction the average for 52 patients was 20.5 mg%. (Nine patients had died, and blood was not obtained from four.) After 2 weeks, if no recognizable extension of the infarction had occurred, the average was still 20.0 mg% for 46 patients. By that time 13 of the original 65 patients had died, one had been discharged, and blood was not obtained from five. After 4 weeks, the average was 16.0 mg% for the 26 patients remaining in the hospital (15 had died and 24 had already been discharged). This level is comparable to that seen in patients with chronic coronary heart disease.

Figure 2 shows the values for phosphatidyl ethanolamine after an acute myocardial infarction, expressed in percentages of total phospholipids. In 70 normal individuals we had previously found that phosphatidyl ethanolamine accounts for 3.0% of the total phospholipids (range 2.0 to 4.0%). In the 70 patients with chronic coronary heart disease the respective figures as already noted were 5.5% (range 3.0 to 9.4%). On the first day after the acute infarction the values for phosphatidyl ethanolamine expressed in percentages of the total phospholipids averaged 10.3% (range 4.8 to 16.2%). Thus in the acute stage of myocardial infarction the share of phosphatidyl ethanolamine of the total phospholipids was about twice as high as in chronic coronary heart disease. On the second and third days after the infarction the percentages declined. They ranged from 5.9 to 13.1% with an average of 9.0% and from 5.3 to 12.8% with an average of 7.3%, respectively. Here again an increase in the values for phosphatidyl ethanolamine was noted in some cases. By the end of the first week phosphatidyl ethanolamine was on the average 7.0% of the total phospholipids; after 2 weeks the average was 6.5% and after 4 weeks it was 5.0%. Thus after a month the phosphatidyl ethanolamine values expressed in percentages of the total phospholipids had returned to the level which we have found in patients with chronic coronary heart disease.

The values for phosphatidyl serine after acute myocardial infarction show the same tendencies as phosphatidyl ethanolamine (fig. 3). On the first day they averaged 33.16 mg% (range 22.96% to 48.3 mg%). In the 70 normal individuals the average was 9.4 mg%.
(range 5.6 mg% to 12.2 mg%), and in the 70 patients with chronic coronary heart disease the average was 24.6 mg% (range 10.24 mg% to 48.6 mg%). Within 24 hours after an acute myocardial infarction the amount of phosphatidyl serine in the plasma was almost 50% higher than in patients with chronic coronary artery disease. On the second and third days the values for phosphatidyl serine began to decrease. They averaged 30.11 mg% on the second day and 26.18 mg% on the third day. After 1 week the levels had decreased to those seen in patients with chronic coronary heart disease.

Figure 4 shows the values for phosphatidyl serine in acute myocardial infarction expressed in percentages of the total phospholipids. On the first day after infarction the average value was 12% of the total phospholipids (ranging from 6.9 to 17.0%) compared with average values of 7.9% in patients with chronic coronary heart disease and 4.1% in normal individuals. On the second day the average value was down to 10.7% (ranging from 6.7 to 15.3%); on the third day it was 10% (ranging between 5.3 to 13.1%). A week after infarction the average value decreased to 9%, with a low of 6.1% and a high of 14.1%. After 2 weeks it was 8.6% (ranging from 4.9 to 12.4%). About 1 month after the incident the average level of phosphatidyl serine was 7.3% (ranging from 5.2 to 9.6%) which is similar to the level in the patients with chronic coronary heart disease.

**Figure 4**

**Discussion**

The levels of phosphatidyl ethanolamine found in the plasma of patients with acute myocardial infarction were 50 to 100% higher than in patients with chronic coronary heart disease, and the levels of phosphatidyl serine were about 50% higher. After the initial few days of the acute attack the values for both cephalins decreased slowly. After 4 weeks the values for phosphatidyl ethanolamine reached the level found in patients with chronic coronary heart disease. The values for phosphatidyl serine reached this level after 1 week.

In acute myocardial infarction as compared with chronic coronary heart disease, phosphatidyl ethanolamine and serine increased not only in absolute values, but also in their ratio to the total phospholipids in the plasma.

The significance of the findings is not clear. Cephalins appear to be intimately involved in the clotting mechanism. Ferguson on the basis of his own experiments concluded that a component which has many analogies to cephalin is of particular significance in the thromboplastic system and that lipid release from platelet tissue or possibly plasma may very well be the long obscure “trigger mechanism” that initiates blood coagulation. Increased amounts of cephalin in the plasma, therefore, may be one of the introductory steps of accelerated blood coagulation. Hence it is of interest to consider the possible pathogenic relationship between increased cephalins and arterial thrombosis with infarction. There is, however, also the possibility that the increase of the cephalins may follow rather
than precede the presumed vascular occlusion. The increase may be simply one of many associated changes in the acute phase of the clinical episode.

Summary

In the plasma of patients with acute myocardial infarction the values for phosphatidyl ethanolamine are on the average 50% to 100% higher than in patients with chronic coronary heart disease and up to 400% higher than in normal individuals. Those for phosphatidyl serine are about 50% higher than in patients with chronic coronary heart disease and up to 300% higher than in normal individuals. Expressed in percentages of total phospholipids, the share of phosphatidyl ethanolamine in acute myocardial infarction is about twice as high as in chronic coronary heart disease and three times as high as in healthy persons. The share of phosphatidyl serine is about 50% higher than in patients with chronic coronary heart disease and also almost 300% higher than in healthy persons. Following the acute incident the values for the cephalins, both phosphatidyl ethanolamine and phosphatidyl serine, decrease slowly. Phosphatidyl ethanolamine reaches the level found in patients with chronic coronary heart disease in about 4 weeks, phosphatidyl serine in about 1 week.

References


There is a divine discontent with the existing order of things which leads to progress. Youth is always insurgent, a builder of images, a dreamer of dreams. When guided by scientific imagination youth builds images to be compared with known facts, and dreams true dreams. Age carries mental scars left by experience which contract and shorten life, but age carries wisdom. Youth and age should travel together; each needs the other for orderly scientific advancement.—W. J. Mayo, Editorial. Surg Gynec Obstet 45: 115, 1927.
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