Serum Lipoproteins in Patients with Intermittent Claudication and Myocardial Infarction

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In the investigation of atherosclerosis it is frequently implied that clinical evidence of involvement of one part of the arterial tree, such as the coronary arteries, indicates a general state of atherosclerosis. Since this view is not necessarily correct, it seemed important to study some features of lipid metabolism in patients whose clinical indication of atherosclerosis was occlusion of an arterial territory other than the coronary, and to compare them with findings in patients with symptoms of coronary artery disease and in subjects with no clinical evidence of arterial disease. Patients with intermittent claudication were chosen. In such patients Barker found a higher serum cholesterol and total lipids than in controls of similar age. However Azen et al. measured low-density lipoproteins in 84 patients with intermittent claudication and found that 57 per cent had normal values and only 25 per cent were definitely outside their normal range.

Material and Methods

Four groups of patients were studied. Group 1 comprised 44 male patients with occlusive arterial disease of the legs. They had clinical evidence of severe involvement of the arteries of both legs, which was confirmed by femoral arteriography. Patients with diabetes mellitus, essential hypercholesterolemia, and those with clinical evidence of a major arterial occlusion within the past 6 months were excluded. Their average age was 61, with a standard deviation of 7.4 years.

Group 2 comprised 61 men who were matched with group 1 for age and who had no symptoms or signs of coronary or peripheral arterial disease.

Their average age was 63, with a standard deviation of 8.1 years.

Group 3 comprised 30 male patients who had had a myocardial infarction 3 to 4 weeks previously and who had no evidence of arterial disease elsewhere. Their average age was 49, with a standard deviation of 7.2 years. They were all on a normal diet, and after an initial 2 days on heparin were receiving phenindione.

Group 4 comprised 30 inmates of a home for elderly men who were studied because of the possible relevance of lack of exercise. They all led a sedentary life and had no symptoms or signs referable to their cardiovascular system. Their average age was 65, with a standard deviation of 8.1 years.

Serum lipoproteins were separated by electrophoresis, stained with Sudan black B, and scanned. Since other workers have found that in coronary artery disease beta lipoproteins are raised and alpha lipoproteins lowered, the beta/alpha ratio was the index measured.

Results

Figure 1 shows the frequencies of distribution of the different beta/alpha lipid ratios in the 4 groups. The mean ratio for each group is shown in table 1 and the ratios are compared in table 2. The mean ratio for patients in group 1 is significantly higher than for the other groups, which do not differ significantly from each other.

The comparison of mean ratios does not fully describe the differences between the groups because the frequency distributions depart somewhat from the normal Gaussian form. Differences between group 1 and the other groups are further shown by differences in modal values and in the relative numbers of rather high ratios in group 1. Nevertheless there is considerable overlap between ratios in the 4 groups.

Since the mean age for group 3 was lower than for group 1, the possibility was consid-
considered that this difference in age might account for the lower lipid ratios in group 3. Calculation showed, however, that there was a significant negative regression between lipid ratios and age in group 3, the ratios decreasing by 0.02 per year from ages 32 to 73. A similar calculation for the patients in the other 3 groups showed no significant regression.

Discussion

These results show that as a group, patients with symptoms of arterial occlusion of the main arteries of the legs differ from patients with symptoms due to occlusion of the coronary arteries and from people of similar age with no symptoms of arterial occlusion, in having relatively high beta/alpha lipid ratios in their blood. Since they differ in the same way from men of similar age whose exercise is restricted for other reasons, this is not simply the consequence of lack of exercise.

The difference between the normal controls and the patients with coronary occlusion is almost significant but 2 points merit consideration. Firstly, Dodds and Mills showed that myocardial infarction is itself associated with significant lipoprotein abnormalities that persist for at least 8 weeks, and since the patients in the present study were investigated 3 to 4 weeks after their myocardial infarction, their lipid ratios may have later returned to lower levels. Secondly, the group of patients with myocardial infarction included many elderly subjects and this would tend to lower the lipid ratio for the group. The significant negative regression between lipid ratios and age in this group is in agreement with the findings of Oliver and Boyd that in coronary artery disease the greatest increase in plasma lipids occurred in the younger age groups. This does not appear to be a feature of patients with intermittent claudication or subjects without symptoms of vascular occlusion.

There are several possible interpretations of these findings. The high beta/alpha lipid ratios in patients with intermittent claudication might reflect more extensive and severe atherosclerosis than exists in patients with myocardial infarction and in those with no clinically evident arterial occlusions. This seems unlikely, since evidence from necropsy and radiologic studies suggests that the populations from which these groups were selected may not differ strikingly in the extent of atherosclerosis in the arteries of the legs. Since the patients with intermittent claudication do, however, differ from comparable people without symptoms in the extent and severity of thrombotic arterial occlusions in their legs, it is possible that their beta/alpha lipid ratios are more directly related to intrarterial thrombosis. It is interesting that fibrinolytic activity in these patients is also markedly depressed compared with patients of the same age without clinical evidence of occlusions, but is normal in patients who had recovered after a myocardial infarction. The groups of patients studied may vary therefore in their liability to intravascular thrombosis.

Conclusive evidence of this would have to come from the study of the natural histories of the 2 diseases. Such studies as are available

Figure 1

Beta/alpha lipid ratios in patients with myocardial infarction, intermittent claudication, and controls.
Table 1
Mean Beta/Alpha Lipid Ratios and Their Standard Deviation

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Mean ratio ± standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Intermittent claudication</td>
<td>44</td>
<td>4.6±0.22</td>
</tr>
<tr>
<td>2. Symptomless controls</td>
<td>61</td>
<td>2.7±0.11</td>
</tr>
<tr>
<td>3. Myocardial infarction</td>
<td>30</td>
<td>3.1±0.24</td>
</tr>
<tr>
<td>4. Sedentary controls</td>
<td>30</td>
<td>2.9±0.17</td>
</tr>
</tbody>
</table>

Table 2
Comparisons of Differences between Mean Beta/Alpha Lipid Ratios

<table>
<thead>
<tr>
<th>Groups compared</th>
<th>Difference between means</th>
<th>Standard error of difference</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 and 2</td>
<td>1.89</td>
<td>0.2455</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>1 and 3</td>
<td>1.46</td>
<td>0.3243</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>1 and 4</td>
<td>1.69</td>
<td>0.2764</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>2 and 3</td>
<td>0.43</td>
<td>0.3619</td>
<td>0.05&lt;p&lt;0.1</td>
</tr>
<tr>
<td>2 and 4</td>
<td>0.20</td>
<td>0.1982</td>
<td>0.2&lt;p&lt;0.3</td>
</tr>
<tr>
<td>3 and 4</td>
<td>0.23</td>
<td>0.2910</td>
<td>0.5&lt;p&lt;0.4</td>
</tr>
</tbody>
</table>

A third possibility is whether atherosclerosis in different arterial territories is governed by different factors. It has been shown that the administration of estrogens will reduce the severity of atherosclerosis in the coronary artery and not in the aorta. The serum cholesterol level was shown to be related to the degree of coronary thrombosis and to the cholesterol content of the coronary artery, but not to the cholesterol content of the aorta. A good correlation was found between age and the severity of atherosclerosis in the femoral artery, but not in the coronary artery. The finding of a high beta/alpha lipid ratio in patients with intermittent claudication may further reflect the fact that the same factors do not necessarily govern the occurrence of occlusive arterial disease in different territories.

Summary

The serum beta/alpha lipid ratios were estimated by electrophoresis in 4 groups of people. These comprised 44 male patients with intermittent claudication; 61 men who were matched for age with the previous group and who were clinically free of cardiovascular disease; 30 male patients who had previously had a myocardial infarction; and a further group of 30 male controls whose physical activity was limited by factors other than disease.

The highest mean serum beta/alpha lipid ratio was found among the patients with intermittent claudication and was very significantly higher than the ratios found among the other 3 groups. The difference in the ratios between the patients with myocardial infarction and the 2 control groups was not significant.

These differences and in particular the difference in the ratios between the patients with myocardial infarction and intermittent claudication are discussed.

Acknowledgment

I wish to thank Professor R. R. H. Lovell for advice and encouragement, and Dr. T. E. Lowe, Director, and Dr. A. J. Barnett, Associate Director, of the Baker Medical Research Institute, Melbourne, where part of this work was commenced.
Summario in Interlingua

Le proportion de lipo de beta a alpha in le sero esseva estimate electrophorettamente in 4 gruppus de subjectos. Istos esseva (1) 44 patientes mascule con claudication intermittente, (2) 61 subjectos mas- cule, appareate in etate con le previe grupp e clinicamente libere de morbo cardiovascular, (3) 30 patientes mascule que habeva recentemente habite un infarcimento myocardial, e (4) 30 subjectos mascule, serviente como grupp de controle, con restriction de activitate physic in consequentia de factores altere que morbos clinic.

Le plus alte valor medie pro le proportion de lipo beta a alpha in le sero esseva incontrate in le patien- tes con claudication intermittente; isto esseva signifi- cativissimemente plus alte que le proporciones tro- vate in le valore 3 gruppus. Le differentia inter le proportiones in patientes con infarcimento myocardial e in le 2 gruppus de controle non esseva significative.

Le differentias observate es discutite, specialmente le differentia inter le proportion in patientes con infarcimento myocardial e illo in patientes con claudication intermittente.

References

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