Lipid profile with paternal history of coronary heart disease before age 40

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Abstract

Serum lipids were measured in children and their parents from 40 families in which the father had a myocardial infarction or coronary heart disease (CHD) before age 40 years. The relationship between physical activity and serum lipid concentrations in the children was also evaluated.

Twenty six men had one or more abnormal lipid value (in mmol/l): total venous cholesterol (TVC) >6.24 , triglycerides >2.55 , low density lipoprotein cholesterol (LDL-C) >4.42 , or high density lipoprotein cholesterol (HDL-C) <0.91 . There were 15 spouses with significant hyperlipidaemia (values above). In the 107 children examined, TVC mean (SD) was 4.68 (1.17), triglycerides 1.4 (0.8), LDL-C 3.0 (1.0), and HDL-C 1.18 (0.28). Altogether 42% of the children had significant hyperlipidaemia. No significant correlation was found between the degree of physical activity of the children and their LDL-C and TVC concentrations. However, a significant positive correlation was found between the degree of physical activity and HDL-C and a significant negative one with triglyceride concentrations.

It is concluded that screening the progeny of young CHD patients is highly productive in identifying young people at excessive risk for future CHD. The data also suggest that promoting high degrees of activity among these children may have a positive influence on risk factors for adult onset CHD.

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Earlier reports have shown that children whose parents had a myocardial infarction at an early age may demonstrate serum lipoprotein abnormalities.^{1 2} Increased total cholesterol and low density lipoprotein cholesterol (LDL-C) concentrations are found to aggregate within certain families in which children exhibit hypercholesterolaemia.³ Increased cholesterol concentrations in childhood are often predictive of those in adult life.⁴ To detect children at high risk, in 1985, the National Institute of Health, USA, recommended a blood cholesterol test for children whose parents, grandparents, or first degree relatives had hypercholesterolaemia or premature coronary

heart disease (CHD) (<50 years of age in men, <60 years of age in women).⁵ Many surveys examining the lipoproteins in the progeny of young men with CHD have followed this recommendation.^{1 2 6-8}

A relationship between physical activity and increased concentrations of high density lipoprotein cholesterol (HDL-C) in both young⁹ and middle aged men has been demonstrated.¹⁰ However, similar studies performed in young children show conflicting data.^{11 12} The present investigation was undertaken to study the lipoprotein fractions in children whose fathers had myocardial infarction or CHD before the age of 40 years. The lipoprotein fractions were analysed in the parents as well. The relationship between physical activity and serum lipid concentrations in these children was also evaluated.

Subjects and methods

Children from 40 families in which the father had a myocardial infarction or CHD before the age of 40 years and were treated in our hospital, were invited to attend the paediatric clinic for a physical examination and serum lipid determination. We included in the study only adults with CHD and angiography proved coronary artery stenosis of more than 70% of one or more major branches. The children were examined by the same physician throughout the study. None of the children had any symptoms and signs of secondary hypercholesterolaemia due to hypothyroidism, nephrotic syndrome, liver disease, or diabetes mellitus. None were receiving any continuous medical treatment. Body weight, height, and blood pressure were recorded. Body mass index, weight/height², was used as an obesity index. Satisfactory dietary intake information was difficult to obtain; however, 80% of the families did not adhere to a low saturated fat-low cholesterol diet. After a 12 hour fast, total venous cholesterol (TVC), triglycerides, and HDL-C were determined in both children and parents. LDL-C was calculated using the standard formula: LDL-C = TVC minus HDL-C minus triglycerides/5. The blood tests were performed using an IL Monarch analyser. Lipid values were reproducible within 5% of true value and the same values were reproducible within 4% of a standard sample. The time interval between the coronary event and the evaluation of the lipid profile was one to two years. We obtained parental histories of additional cardiovascular risk factors such as diabetes, hypertension, and smoking.

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Table 1 Lipoprotein concentrations (mmol/l) in 34 men with early CHD [number in parenthesis shows number of men studied]

	Acceptable	Borderline	High
Total cholesterol	<5.20 [7]	5.20–6.24 [10]	>6.24 [17]
Triglycerides	<1.95 [8]	1.95–2.55 [10]	>2.55 [16]
LDL-C	<3.38 [8]	3.38–4.42 [10]	>4.42 [16]
HDL-C	>1.17 [9]	0.91–1.17 [14]	<0.91 [11]

Table 2 Lipoprotein concentrations (mmol/l) in 40 spouses of 34 men with early CHD [number in parenthesis shows number of spouses studied]

	Acceptable	Borderline	High
Total cholesterol	<5.20 [19]	5.20–6.24 [13]	>6.24 [8]
Triglycerides	<1.95 [29]	1.95–2.55 [3]	>2.55 [8]
LDL-C	<3.38 [17]	3.38–4.42 [17]	>4.42 [6]
HDL-C	>1.17 [27]	0.91–1.17 [11]	<0.91 [2]

Children were classified into four groups according to their physical activity including gymnastics, swimming, soccer, basketball, and swimming. In group 1 there was no physical activity (16 children); group 2, <3.5 hours/week of physical activity (42 children); group 3, 3.5–7 hours/week of physical activity (31 children); and group 4, >7 hours/week physical activity (18 children).

The study was approved by the research and human ethics committees of our hospital.

STATISTICAL METHODS

Results are presented as the mean (SD) in mmol/l. The influence of physical activity on lipid concentrations was assessed by χ^2 and Wilcoxon rank tests; *p* values <0.05 were considered significant. The relationship between TVC and LDL-C concentrations was evaluated by linear regression analysis.

Results

Three fathers from 40 families had died from myocardial infarction and three fathers refused to participate. The age of the 34 fathers tested for hyperlipidaemia was 38 (2.1) (range 31–41) years. Twenty nine patients had a myocardial infarction: 10 of the anterior wall, 16 of the inferior wall, one of the lateral wall, and two of the posterior wall; five patients suffered from severe CHD. The lipid profile of the 34 men is summarised in table 1. Only eight patients had normal lipid concentrations. Twenty six men (77%) had one or more abnormal value of the following (in mmol/l)

TVC >6.24, triglycerides >2.55, LDL-C >4.42, or HDL-C <0.91. TVC concentration in the whole group was 6.50 (1.50), triglycerides 2.80 (1.35), LDL-C 4.62 (1.40), and HDL-C 1.10 (0.28). There was no significant difference between the lipid profile in the men with anterior compared with inferior wall myocardial infarction. Examining coronary risk factors in these 34 men, 27 of them (79%) were heavy smokers (more than 20 cigarettes/day for more than three years preceding the coronary event), 22 had a positive coronary family history, seven had hypertension, and six were obese (body mass index >30 kg/m²). There was no correlation between the body mass index values on one hand and the TVC, triglycerides, LDL-C, and HDL-C values on the other.

TVC concentrations in the 40 spouses were (in mmol/l) 5.46 (1.35), triglycerides 1.65 (0.78), LDL-C 3.60 (1.20), and HDL-C 1.30 (0.30). The lipid profile of the 40 spouses is summarised in table 2. There were 15 spouses (38%) with significant hyperlipidaemia: TVC >6.24, triglycerides >2.55, LDL-C >4.42, or HDL-C <0.91 or in any combination. No spouse had CHD. Six of the mothers were obese (body mass index >30 kg/m²). There was no correlation between the body mass index values on one hand and the TVC, triglycerides, LDL-C, and HDL-C values on the other.

In the 34 families where fathers were tested for hyperlipidaemia, we identified 107 children aged 12 (4.6) (range 2–20) years. There were 59 boys and 48 girls. TVC concentration was (in mmol/l) 4.68 (1.17), triglycerides 1.40 (0.80), LDL-C 3.00 (1.00), and HDL-C 1.18 (0.28). The lipid profile of the children is summarised in table 3. Altogether 42% of the children had significant hyperlipidaemia (above the 95th centile): TVC >5.20, LDL-C >3.38, triglycerides >1.95 or HDL-C <0.91 or in any combination. In 26 families, at least one child in every family was found to have a lipoprotein abnormality. In eight families, both parents had lipoprotein abnormalities, in 18 families only the father, and in three families only the mother was found to have hyperlipidaemia. Only one child was obese (body mass index >27 kg/m²). A positive correlation was found between TVC and LDL-C levels (*r*=0.8, *p*<0.001). No correlation was found between the age and sex of the children and lipid concentrations.

No significant correlation was found between the degree of physical activity of the children and their LDL-C and TVC levels (figure). However, a significant positive correlation was found between the degree of physical activity and HDL-C (*p*<0.05) and a significant negative one with triglyceride concentrations (*p*<0.05) (figure). There was a strong association between the HDL-C in children whose physical activity corresponded to groups 2–4 and their fathers. However, no such association was found in the children with no physical activity (group 1). In those children, the lack of physical activity was the main reason for their low HDL-C concentration.

Table 3 Lipoprotein concentrations (mmol/l) in 107 children whose fathers had early CHD and lipoprotein concentrations measured (*n*=34) [number in parenthesis signifies the number of children studied]

	Acceptable	Borderline	High or low for HDL-C	Very high
Total cholesterol	<4.42 [46]	4.42–5.17 [35]	5.20–6.24 [18]	>6.24 [8]
Mean (SD)	3.80 (0.49)	4.76 (0.23)	5.67 (0.36)	7.56 (0.80)
Triglycerides	<1.50 [70]	1.50–1.92 [22]	1.95–2.55 [11]	>2.55 [4]
Mean (SD)	1.00 (0.24)	1.68 (0.13)	2.16 (0.11)	4.50 (1.70)
LDL-C	<2.60 [37]	2.60–3.35 [43]	3.38–4.16 [12]	>4.16 [15]
Mean (SD)	2.10 (0.38)	3.00 (0.21)	3.60 (0.16)	4.80 (0.80)
HDL-C	>1.17 [49]	0.91–1.17 [40]	<0.91 [18]	
Mean (SD)	1.46 (0.18)	1.00 (0.08)	0.80 (0.05)

Distribution of the lipid concentrations in the four groups of children according to their degree of physical activity (group 1, no physical activity; group 4, the highest level of activity, see methods section).

Discussion

There are only a few studies^{13 14} which examined the lipid profile in children from kindreds with premature parental myocardial infarction. In our study, we confirmed the findings of a high incidence of raised total cholesterol and triglyceride in the progeny of young men (under 40 years) with CHD.

We performed a cholesterol routine surveillance study of 809 children 6 to 14 years of age chosen at random. The mean (SD) cholesterol concentration was 3.74 (0.6) mmol/l (unpublished data). The mean cholesterol concentrations in the present study, which represents a high risk group of children for the development of CHD, was significantly higher, 4.68 (1.25) mmol/l ($p < 0.001$). In addition, we have also shown that abnormalities of the lipoprotein fractions with raised LDL-C and diminished HDL-C concentrations are frequently present in these children. Forty two per cent of the offspring had an abnormality of total lipids or lipoproteins. Prospective studies have clearly shown that raised plasma cholesterol is associated with an increased risk for the development of myocardial infarction or coronary artery disease.^{15 16} Because of the significant correlation of total plasma cholesterol and LDL-C found in our study ($r = 0.8$), LDL-C may serve as a strong indicator of CHD.

We noted a higher incidence of hyperlipoproteinaemia (77%) in young male survivors of coronary disease than in other studies.^{2 13 14} Different arbitrary limits of normal lipid values as well as differing laboratory methodology, study design, and environmental differences between populations may influence the prevalence of hyperlipoproteinaemia among the various studies. Interestingly, no negative correlation was found in our study between body mass index and HDL-C values in both parents contrary to other studies.^{17 18} A very high incidence of heavy smokers (79%) was also found in the men with premature CHD. In the study of Nora *et al* the highest risk ratio for early onset ischaemic heart disease was associated with a positive family history for ischaemic heart disease.¹⁹

As with previous studies^{11 20 21} no correlation was found between the degree of physical activity and cholesterol or LDL-C concentrations. However, the degree of physical activity correlated inversely with HDL-C concentrations. Moreover, lack of physical activity was the main contributor to the low HDL-C, being more significant than genetic influence. Klesges *et al* found no significant relationships between physical activity and CHD risk variables in their group of preschool children, and suggested that the relationship between physical activity and health outcome variables may be weaker among children than adults.²² Our finding of 17% of children with low HDL-C concentrations in families with early onset CHD, emphasises the importance of physical activity and fitness among these high risk children in preventing adult onset CHD. Confirming other studies,^{23 24} we found that children with lower physical activity had higher triglyceride concentrations.

We conclude that screening the progeny of young coronary artery disease patients is highly productive in identifying young people at excessive risk for future coronary artery disease. Early identification of this young high risk population offers an opportunity for early initiation of preventive measures. We also found that cardiovascular fitness appears to have a positive influence on HDL-C and higher physical activity was associated with lower triglyceride concentrations. These data suggest that promoting high degrees of activity among children from a high risk group for CHD may have a positive influence on risk factors of adult onset CHD.

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