

Risk factors in childhood diabetes mellitus

L BARTA, A CZINNER, Mária TICHY, Magdolna BEDŐ

First Department of Paediatrics, Semmelweis University Medical School, and
National Institute of Nutrition, Budapest

The quotients total cholesterol/HDL-cholesterol and free fatty acid/albumin in serum were examined in various groups of diabetic patients and the changes of the quotients induced by various forms of physical activity were then registered. Both total cholesterol/HDL-cholesterol and free fatty acid/albumin were increased in patients with unsatisfactory control of diabetes. Low albumin levels were only seen in cases with very poor control or in cases afflicted by complications. Increased muscular activity unvariably led to a fall in the value of total cholesterol/HDL-cholesterol while in children with adequate control but performing little physical exercise the quotient of free fatty acid/albumin was low and total cholesterol/HDL-cholesterol was increased. In addition to the quotient of total cholesterol/HDL-cholesterol also the quotient of free fatty acid/albumin is a sensitive indicator of the diabetic condition.

In a previous study [1] we showed by fluorescent angiography (FA) that vascular changes of the retina may occur in the earliest stage of childhood diabetes: in 50% of cases with a duration of diabetes less than 5 years FA demonstrated the presence of microaneurysms. These findings have been confirmed by others [7]. Good control of diabetes, however, markedly reduces the incidence of microaneurysms [2].

In this study we have attempted to answer the question how far the changes in risk factors influencing the onset of angiography are followed by changes in the diabetic condition.

In the pathogenesis of arteriosclerosis an important role has been ascribed to the lipid and lipoprotein status, notably to the high value of the total cholesterol/high density lipo-

protein cholesterol quotient (LDL-C/HDL-C) [10]. In addition, changes in haemostasis, due to alterations in the prostacycline system, also play a decisive part in the appearance of vascular phenomena. Prostacycline (PGI_2) inhibits platelet aggregation, and this inhibition is abolished by FFA, which enhances PGI_2 catabolism. Albumin exerts an opposite effect.

In the experiments of Reinila [9] on diabetic rats the value of the free fatty acid/albumin quotient was as high as 2.3–3.3 in the animals affected by vascular changes, 1.4–1.8 in diabetic animals free from blood vessel alterations, and 0.6–1.1 in healthy controls.

To our present knowledge, both increased values of total cholesterol/HDL-cholesterol and FFA/albumin

carry an angiological risk. The value of these quotients has been determined in various groups of diabetic children to see how far the unfavourable circumstances in diabetic control led to an increase in them.

MATERIAL AND METHODS

Group 1 comprised 17 diabetic children prone to acidosis, needing frequent hospitalisation, in whom good control could not be achieved; their FFA/albumin quotient was compared with that of 10 healthy children.

In the second course of studies 10 children with reasonable control of diabetes (daily glucose output less than 20 g, no acetonuria) and 28 children with less satisfactory control (daily glucose output over 20 g, occasional acetonuria) were examined.

The changes in the value of the quotients induced by increased physical activity in a camp were studied in 16 children of Group 3.

The same changes were examined in 28 children going to school, exerting little physical effort and under good diabetic control.

Also, the circadian rhythm of total cholesterol/HDL-cholesterol and FFA/albumin was determined in healthy and diabetic children ($n = 8$).

A total of 107 diabetic children participated in the study, 45 boys and 62 girls, aged between 9 and 15 years. All were treated with monocomponent insulin (Actrapid MC and Monotard). Most of them received insulin twice daily. The main duration of diabetes was 2.7 and 2.58 years, respectively.

Free fatty acids were determined according to the method of Dole and Meinerts [3], albumin was measured by radial immune diffusion, cholesterol and HDL-cholesterol enzymatically, triglyceride by the method of Laurell [6], blood glucose by the o-toluidine method. All results were expressed in mmol/l.

In eight children LDL-cholesterol was determined by Friedwald's formula, from this the changes in LDL-cholesterol/HDL-cholesterol were calculated and compared with those in total cholesterol/HDL-cholesterol. The direction and magnitude of the changes in both quotient values proved to be identical, therefore the lipid status was characterised by the value of the total cholesterol/HDL-cholesterol quotient, in accordance with other authors [10]. In our experience the upper limit of the normal range was 5.5 for total cholesterol/HDL-cholesterol and 1.4 for FFA/albumin.

RESULTS

In the 17 children with poorly controllable diabetes HDL-cholesterol was 0.92 ± 0.31 (mean $\pm$ SD), serum total cholesterol was 7.4 ± 2.7 mmol/l. The quotient FFA/albumin was markedly increased because of a considerably low albumin level (free fatty acid/albumin was 1.53 ± 0.72 in the 17 diabetics while 0.60 ± 0.12 in the healthy controls; serum albumin of the diabetics was 0.48 ± 0.17 , that of the healthy children, 0.58 ± 0.12).

As can be seen in Table I, increased FFA and decreased HDL-cholesterol were the most sensitive indicators of poor control of diabetes; as a consequence, both quotients, FFA/albumin and total cholesterol/HDL-cholesterol, showed increased values.

Table II demonstrates that a significant fall in FFA/albumin and total cholesterol/HDL-cholesterol was achieved by a three-week camp offering much physical exercise.

In children who have access to physical activity only during the

TABLE I

Risk factors in healthy controls and diabetic children with good or less satisfactory control

Group	FFA	Albumin	FFA/albumin	HDL-C	Total cholesterol/HDL-C
Controls n = 10	0.344 ± 0.094	0.58 ± 0.12	0.60 ± 0.12	1.29 ± 0.32	3.60 ± 1.03
Diabetic, good control n = 10	0.511 ± 0.099	0.63 ± 0.12	0.80 ± 0.38	1.15 ± 0.23	4.39 ± 0.52
Diabetic, less satisfactory control n = 28	$0.897 \pm 0.127^{**}$	0.61 ± 0.36	1.47 ± 0.58	0.98 ± 0.32	$5.98 \pm 1.95^*$

* $p < 0.05$
 ** $p < 0.001$

TABLE II

Risk factors during camping

n = 16	FFA/albumin	Total cholesterol/HDL-C	HDL-C
Before camping	1.35 ± 0.23	5.73 ± 1.50	0.86 ± 0.19
After camping	$0.88 \pm 0.21^{**}$	$4.87 \pm 1.09^*$	$1.03 \pm 0.21^*$

* $p < 0.001$
 ** $p < 0.01$

TABLE III

Risk factors during a period of decreasing physical activity

n = 28	FFA/albumin	Total cholesterol/HDL-C
Satisfactory muscular activity	1.30 ± 0.48	5.70 ± 1.40
Decreasing muscular activity (school)	1.08 ± 0.30	7.46 ± 2.50

} $p < 0.001$

summer holidays but have much less elbowroom when going to school and whose diabetes could satisfactorily be controlled, a fall in FFA/albumin and a very marked increase in total

cholesterol/HDL-cholesterol were observed during a three-month period.

Figure 1 shows the circadian rhythm of the quotients. Total cholesterol/HDL-cholesterol exhibited a

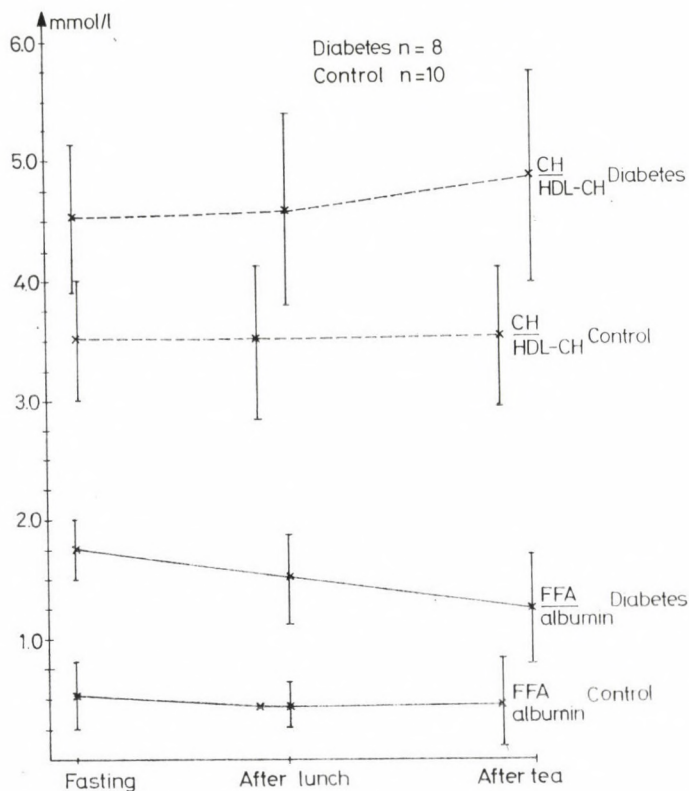


FIG. 1

moderate increase over the day while FFA/albumin a significant fall; this latter phenomenon was due to the decrease of the level of free fatty acids caused by the effect of insulin. Blood glucose was 12.96 ± 1.78 , 10.54 ± 5.34 and 11.90 ± 3.97 mmol/l at the corresponding occasions.

DISCUSSION

As a consequence of circadian oscillations the lowest values of total cholesterol/HDL-cholesterol and the highest ones of FFA/albumin could

be observed in the fasting subjects. The favourable decrease in total cholesterol/HDL-cholesterol could be achieved by enhanced physical exercise, in addition to good control of diabetes. In case of unsatisfactory physical activity, adequate insulin treatment resulted in a favourable change of FFA/albumin but the mean of total cholesterol/HDL-cholesterol increased in consequence of a fall in HDL-cholesterol. On increased physical exercise, both the FFA/albumin and total cholesterol/HDL-cholesterol ratios decreased. This exercise-induced increase in HDL-cholesterol

could be registered in both healthy and obese non-diabetic subjects [10].

There are few publications on the FFA/albumin quotient although in vitro studies [5, 8] and animal experiments [9] have pointed to its significance in the pathogenesis of vascular changes. Low albumin values accompanied by increased free fatty acid levels can be expected in complicated and poorly controlled cases. In our material, the lowest value, 0.33 mmol/l, has been encountered in a case affected by diabetes complicated by coeliac disease. It is well known that the FFA level in diabetics is a consequence of insulin therapy. In the overwhelming majority of our cases the albumin level was normal and the increase in the value of the FFA/albumin quotient was due to a high FFA level.

In respect to the prevention or postponement of angiopathy or to a deceleration of its progression it may be important to keep the value of the FFA/albumin quotient within normal limits and, doing this, the albumin levels must also be considered.

Risk factors are obviously present in childhood diabetes but it is difficult to judge their role in the pathogenesis of angiopathy. Constitution must here play an important role:

FA studies have shown that even the best control of diabetes cannot always prevent the appearance of microaneurysms in childhood.

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Prof L BARTA MD
Bókay J. u. 53
H-1083 Budapest, Hungary