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Short Communications

Exercise-Induced Proteinuria in Children and Adolescents with Type 1 (Insulin Dependent) Diabetes

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Summary. The urinary excretion of albumin and β_2-microglubulin was measured by radioimmunoassay in 64 children and adolescents with Type 1 (insulin dependent) diabetes and in 68 non-diabetic subjects aged from 9 to 19 years. At rest the albumin excretion of the diabetic subjects did not differ from that of the non-diabetic children and adolescents but during exercise the albumin excretion was significantly higher in children and adolescents with Type 1 diabetes ($p < 0.02$). The excretion rate of β_2-microglobulin in diabetic subjects did not differ from that of the healthy subjects. Both at rest and during exercise the albumin excretion rate was highest in those diabetics with poorest metabolic control of their disease.

Key words: Exercise, albuminuria, β_2-microglobulin, Type 1 diabetes, childhood.

By using sensitive methods and certain provocation tests, slight but clearly abnormal albuminuria can be detected in adults with Type 1 (insulin dependent) diabetes shortly after the onset of their disease [1].

In order to see if there were any abnormal protein leakage in the early course of Type 1 diabetes in children and adolescents, we examined urinary excretion of albumin and β_2-microglobulin in diabetic and healthy subjects aged from 9 to 19 years.

Subjects and Methods

Subjects

Sixty-four children and adolescents with Type 1 diabetes and 68 healthy schoolchildren were examined. The mean age of the diabetics was 13.7 years and that of the non-diabetic subjects 13.9 years. There was an equal number of boys and girls in the group of diabetics, and 39 boys and 29 girls in the control group. The duration of diabetes ranged from one week to 15.1 years with a mean of 6 years. None of the subjects had constant proteinuria, but 13 diabetics (20%) showed occasional positive Albustix readings in their daily urine samples. Serum creatinine of the diabetic subjects ranged from 48 to 91 μmol/l.

Exercise Protocol

After emptying their bladders the subjects first lay down for 10 min and then stood for another 10 min, after which a pre-exercise urine sample was collected. The exercise test was performed on an electrically-braked bicycle ergometer (Godart, Netherlands) and lasted for 16 min. The work load was increased every fourth minute, so that the heart rate would be 170–200 beats/min at the end of the exercise. After the exercise the subjects stayed on the bicycle for 3 min and then lay on a bed for an additional 10 min, after which the second urine sample was collected. The heart rates and blood pressures were recorded every 2 min.

Biochemical Methods and Statistics

Urinary albumin was measured by a double antibody radioimmunoassay [2]. β_2-microglobulin was also measured radioimmunologically using a commercial kit (Phadebas, Pharmacia, Sweden). If the pH of the urine sample was 5.5 or less, it was immediately adjusted to 6–7 with a few drops of NaOH 2 mol/l. Blood haemoglobin A_1 (HbA_1) was determined by ion-exchange chromatography [3]. The differences in the excretion rates of albumin and β_2- microglobulin between the diabetic and non-diabetic subjects were tested by Student's t-test, using logarithmic values of the excretion rates because they corresponded better with a log normal than a normal distribution. The arithmetic mean of all HbA_1 determinations made within one year of the exercise test was used as a measure of the metabolic control of diabetes.

Results

The heart rates at the end of the exercise were 185 ± 7 beats/min (mean ± SD) in diabetic and 185 ± 6 beats/min in non-diabetic subjects, indicating an

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Table 1. The urinary excretion rates of albumin and β_2-microglobulin before and during exercise related to body surface area in diabetic and non-diabetic subjects

	Albumin excretion ($\mu g.min^{-1}.m^{-2}$)					β_2-Microglobulin excretion ($ng.min^{-1}.m^{-2}$)				
	No. of subjects	Before exercise		During exercise		No. of subjects	Before exercise		During exercise	
		Geometric mean	Range	Geometric mean	Range		Geometric mean	Range	Geometric mean	Range
Diabetics										
Total	64	6.5	0.4–778	14.4[c]	1.7–415	45	52.0	0.6–1760	48.8	0.5–2150
Sporadic proteinuria[a]	13	20.7[b]	1.9–772	36.9[b]	2.5–415	10	99.4[b]	21.3–471	118.0[b]	47.6–328
No proteinuria	51	4.8	0.4–21.3	11.3	1.7–172	39	44.1	0.6–1760	40.3	0.5–2150
Non-diabetics	68	4.9	0.3–134	8.6	0.2–92.8	45	36.0	3.3–321	28.5	3.4–306

[a] Proteinuria documented by Albustix. Statistically significant differences between diabetic and non-diabetic subjects are indicated: [b] $p < 0.01$; [c] $p < 0.02$

equal amount of effort in both groups. The maximal systolic blood pressure in the diabetics was 168 ± 25 mmHg and in the non-diabetic subjects 167 ± 23 mmHg.

The urinary excretion rates of albumin and β_2-microglobulin at rest and during exercise are presented in Table 1. The mean excretion rate of albumin rose significantly during exercise in both groups ($p < 0.001$) although there were 21 diabetic (31%) and 13 non-diabetic subjects (20%) whose excretion rate of albumin decreased from rest to exercise. The urinary excretion rate of β_2-microglobulin did not increase during exercise in either group. There was no difference in albumin excretion rate before the exercise between the diabetic and non-diabetic subjects, but during exercise the excretion rate of albumin was significantly higher in the diabetic than the non-diabetic subjects ($p < 0.02$). The geometric mean of urinary albumin/β_2-microglobulin ratios was 123 at rest in the diabetic and 159 in the non-diabetic subjects. During the exercise this ratio was 310 in diabetics and 357 in the healthy subjects. Those diabetics who occasionally showed Albustix-positive proteinuria had a heavier albumin excretion than other diabetics, both at rest and during exercise ($p < 0.005$). In addition, urinary excretion of β_2-microglobulin was significantly increased from normal in these diabetics ($p < 0.01$). However the urinary albumin/β_2-microglobulin ratio of these subjects did not differ from that of the healthy subjects (geometric mean 175 at rest, 315 during exercise). The duration of diabetes did not correlate with albumin excretion at rest, but there was a weak correlation between exercise-induced albuminuria and duration ($r = 0.27$, $p < 0.05$). The correlation between urinary albumin excretion and HbA_1 concentration in the diabetics was significant both at rest ($r = 0.32$, $p < 0.02$) and during exercise ($r = 0.43$, $p < 0.001$). There was a weak but significant correlation between the systolic blood pressure and exercise-induced albuminuria in the diabetics ($r = 0.38$, $p < 0.005$).

Discussion

The results of the present study show that by using sensitive methods and exercise provocation, slight albuminuria, as a sign of renal dysfunction, can be detected in cases of Type 1 diabetes even in childhood. As in adults, the exercise-induced proteinuria in young diabetics is of the glomerular leakage type, as indicated by the increased urinary albumin/β_2-microglobulin ratio during exercise [4]. The extent of albumin leakage into the urine seems to be primarily dependent on metabolic control of the disease. Physical exercise caused a reduction of renal blood flow, which has been suggested as a cause of exercise-induced proteinuria in healthy subjects [5]. The permeability of the glomerular filter to dextran molecules has been shown not to be altered in early diabetes [6]. On the other hand, it has been shown that the glomerular filtration surface is increased in diabetics with poor metabolic control [7].

It seems reasonable to suggest that the exercise-induced reduction in renal blood flow combined with the increased filtration area and perhaps an elevated transcapillary pressure, causes accentuated protein leakage during exercise in diabetic subjects. This renal dysfunction may not be permanent, because it has been found in adult diabetics that exercise-induced albuminuria can be reversed to normal by improving the metabolic control of Type 1 diabetes [8].

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