# EFFECT OF THE EXERCISE TEST ON ALBUMINURIA, BLOOD PRESSURE AND BLOOD GLUCOSE IN TYPE I (INSULIN-DEPENDENT) DIABETIC PATIENTS

PETER PONŤUCH, JURAJ VOZÁR, HELENA KRATOCHVÍL'OVÁ

*I. interná klinika, Lekárska fakulta Univerzity Komenského, Bratislava, Czechoslovakia*

Clinical diabetic nephropathy with proteinuria, hypertension and decline in renal function is a serious complication of diabetes mellitus. It tends to develop in 30-40% of type I diabetic patients after 15-20 years of diabetes[1, 12]. Increased urinary albumin excretion without clinical proteinuria is considered to be a reliable indicator for the development of persistent proteinuria[18, 26]. The change in albuminuria induced by an exercise test was originally studied ten years ago in the search for early diagnostic methods[20, 27]. Since that time other authors have published their results which at times have turned out to be controversial[3, 4, 7, 11, 14, 23, 30]. Nevertheless, the test revealed certain changes in albumin excretion and in systemic hemodynamics in the diabetic patients studied[9]. The aim of our study was to observe urinary albumin excretion rate (UAER), arterial blood pressure and blood glucose during the exercise in type I diabetic patients and in healthy subjects and to explore the relationship between these parameters.

## MATERIALS AND METHODS

In our study, 29 male type I (insulin-dependent) diabetic patients (age range 16-46 years) who had Heptaphan negative urine for proteinuria and normal serum creatinine concentration and 13 healthy subjects (age range 18-43 years) were examined. The diabetic patients were subdivided into two groups according to the resting UAER value determined in the two pre-exercise periods in supine position. Group A included 19 diabetic patients with normal resting UAER $\leq$ 16 μg/min; Group B included 10 diabetic patients with elevated resting UAER (16 < UAER < 126 μg/min). The cut-off point between normoalbuminuria and microalbuminuria is consistent with that of MOGENSEN and CHRISTENSEN[19].

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| | n | age (years) | weight (kg) | glycosylated hemoglobin (μmol f/g Hb) | serum creatinine (μmol/l) |
|---|---|---|---|---|---|
| healthy subjects | 13 | 31 (22-36) | 74 (70-77) | 3.7 (3.1-4.2) | 87.3 (79.8-106.9) |
| diabetic patients with resting UAER ≤ 16 μg/min | 19 | 30 (20-36) | 73 (65-77) | 7.2 (5.9-8.1) | 96.4 (87.3- 99.2) |
| diabetic patients with resting 16 < UAER < 126 μg/min | 10 | 32 (22-35) | 68 (64-80) | 7.7 (7.1-8.9) | 102 (80.9-108.5) |

Tab. 1 - Clinical characteristics of healthy subjects and diabetic patients. UAER = urinary albumin excretion rate. Median and 95% confidence limits are shown.

There was no significant difference in age, weight and serum creatinine concentration between healthy subjects and both groups of diabetic patients (tab. 1). Group B diabetic patients had longer duration of diabetes but the difference was not significant (tab. 2). The groups of diabetic patients did not differ in age at onset of diabetes, daily insulin dose and fasting serum C-peptide concentration (tab. 2). The 24-h UAER was calculated as the arithmetic mean from at least three urine collections during normal daily physical activity. Systolic (SBP) and diastolic (DBP) blood pressure were measured auscultatorily during previous four check-ups by conventional sphygmomanometer with cuff attached to the right arm in sitting position after 10 min rest.

*The exercise test* - All subjects were studied as outpatients. They came to the hospital in the morning in a fasting state without having taken their morning insulin. While still at home they were asked to drink 0.5 l of water and later continued drinking 0.3 l of water every 20 min in our laboratory. The test was started once the steady state of water diuresis had been achieved[28]. It was divided into six periods (every period lasted 20 min): two pre-exercise resting periods, two exercise periods and two post-exercise resting periods. Every period began with water intake and finished with urine collection. All subjects

| | n | duration of diabetes (years) | onset of diabetes (years) | daily dose insulin (IU) | fasting serum C-peptide (ng/ml) | mean fasting blood glucose (mmol/l) |
|---|---|---|---|---|---|---|
| diabetic patients with resting UAER ≤ 16 μg/min | 19 | 6 (3-13) | 20 (15-28) | 56 (44-64) | 0.09 (0-0.25) | 10.3 (8.0-14.2) |
| diabetic patients with resting 16 < UAER < 126 μg/min | 10 | 11.5 (6-17) | 20 (8-27) | 48 (44-68) | 0.06 (0-0.24) | 12.4 (6.3-15.4) |

Tab. 2 - Clinical characteristics of diabetic patients. UAER = urinary albumin excretion rate. Median and 95% confidence limits are shown.

| | n | $\overline{SBP}$ (mmHg) | $\overline{DBP}$ (mmHg) | $\overline{UAER_{24}}$ (mg/24h) |
|---|---|---|---|---|
| diabetic patients with resting UAER ≤ 16 μg/min | 19 | 125 (110-132) | 80 (73-86) | 13.8 (9.1-19.9) |
| diabetic patients with resting 16 < UAER < 126 μg/min | 10 | 140 (118-146) | 81 (73-96) | 32.9* (14.2-50.4) |

Tab. 3 - Blood pressure and albuminuria in diabetic patients during previous check-ups. $\overline{SBP}$, $\overline{DBP}$ = mean systolic and diastolic blood pressure calculated as arithmetic mean from four previous outpatient check-ups. $\overline{UAER_{24}}$ = mean 24-h urinary albumin excretion rate calculated as arithmetic mean from at least 3 urine collections during normal daily activity. Median and 95% confidence limits are shown. *p<0.05.

were exercised on an electrically cycling braked ergometercycle (Jaeger, FRG) in supine position with a work load of 75 W (450 kpm/min) for 20 min and with a work load of 100 W (600 kpm/min) for 10 min (0-5 min and 10-15 min of the second exercise period). They spent the resting periods in a sitting position. We changed the original exercise protocol of MOGENSEN et al.[20] in the second exercise period due to the limited working capacity of our diabetic patients. Immediately before and after exercise the venous blood sample for blood glucose assay was drawn. After completing the test, the diabetic patients ate and received their insulin dose. SBP and DBP during exercise were measured auscultatorily by conventional sphygmomanometer with cuff attached to the right arm in supine position. We considered phase V for DBP. Blood pressure was monitored at 10 min of each resting period, at 5, 10, 15 and 20 min of the first exercise period and at 5 and 15 min of the second exercise period. SBP and DBP during every exercise period were calculated as the arithmetic mean of all values measured. Heart rate was monitored on cardiomonitor Tesla LKM 210, Czechoslovakia. The percentage value of maximal heart rate in relation to age (% MHR) was calculated[24].

All persons studied were informed and gave their consent. The test protocol was approved by the Hospital Board.

*Laboratory methods* - Glycosylated hemoglobin was assayed by a spectrophotometric method using 2-thiobarbituric acid (Lachema, Czechoslovakia). Blood glucose was determined by the enzymatic GOD method (Lachema, Czechoslovakia). Urinary albumin was assessed by a modified electroimmunodiffusion method[15]. C-peptide was assayed by RIA method (Biodata, Sweden) and serum creatinine by a kinetic reaction (Lachema, Czechoslovakia).

*Statistical methods* - For statistical analysis the Kruskal-Wallis test with Neménýi contrast testing and Friedman two-way analysis of variance with Wilcoxon-Wilcox contrast testing were used. For estimation of the relationship between two independent variables, correlation coefficients were determined and between independent and dependent variables regression coefficients were determined. The approach to the biometric design of the experiments and to the statistical processing of data is that of MIKULECKÝ[17].

## RESULTS

*Data obtained from previous outpatient check-ups and in the resting state before exercise*

The groups of diabetic patients did not differ in the mean fasting blood glucose concentration found at previous four check-ups, in pre-exercise blood glucose concentration and in pre-exercise glycosylated hemoglobin concentration (tabs 1, 2 and 4). Group B had a significantly higher mean 24-h UAER, as calculated from at least three urine collections during normal daily activity compared to group A ($p<0.05$) (tab. 3).

The groups of diabetic patients and healthy subjects did not differ significantly in pre-exercise resting SBP and DBP, although these values were moderately higher in group B (figs 1 and 2). Neither could we find any significant difference between the two groups of diabetic patients in mean SBP and DBP calculated as arithmetic mean from previous four outpatient measurements (tab. 3). Pre-exercise resting heart rate was higher in Group B compared to healthy subjects ($p<0.05$), however no difference of this parameter was seen between the two groups of diabetic patients (tab. 4).

*Data obtained during the exercise test*

Maximal heart rate during the constant work load varied in diabetic patients and in healthy subjects (tab. 4). However, there was no significant difference between the two groups of diabetic patients in % MHR, but there was a difference between healthy subjects and both diabetic groups ($p<0.001$) (tab. 4).

In our study UAER increased during the exercise test in the two groups of diabetic patients and in the healthy subjects as well. Group B showed the highest rise in UAER (fig. 3). The significant difference between healthy subjects and Group B in UAER remained on the same level ($p<0.001$) during the pre-exercise resting period and during the work load of 75 W and 100 W, but the difference between the two groups of diabetic patients decreased with increasing work load (fig. 3). A significant regression was found between resting UAER (UAER-p) and its relative increase during exercise ($\Delta$UAER) in Group B at the work load of 75 W ($r = 0.82$, regression equation: $\Delta UAER = -16.5 + 2.05 \cdot$ UAER-p, 95%

| | n | resting heart rate (beats/min) | maximal heart rate (beats/min) | % MHR | pre-exercise blood glucose (mmol/l) | post-exercise blood glucose (mmol/l) | resting urine flow (ml/min) | urine flow at 100 W (ml/min) |
|---|---|---|---|---|---|---|---|---|
| healthy subjects | 13 | 56 (50-68) | 120 (110-132) | 70 (64-77) | 4.7 ( 4.4- 4.8) | 4.3 ( 3.9- 4.6) | 16 (13.5-17.8) | 12.6 (10.4-15.2) |
| diabetic patients with resting UAER ≤ 16 µg/min | 19 | 62 (56-70) | 152** (140-162) | 82** (78-92) | 10.9 ( 7.9-18.9) | 13.8 ( 6.8-21.6) | 12.5* ( 9.5-14.5) | 10.4* ( 7.6-12.6) |
| diabetic patients with resting 16 ≤UAER<126 µg/min | 10 | 70* (52-82) | 152** (140-162) | 83** (76-91) | 15.5 (11.2-19.7) | 16.6 (10.9-21.9) | 11.2* ( 9.5-15.5) | 9.1* ( 4.4-11.6) |

Tab. 4 - Heart rate, blood glucose and urine flow during the exercise test in healthy subjects and in diabetic patients. UAER = urinary albumin excretion rate. %MHR = % value of maximal heart rate in relation to age. Median and 95% confidence limits are shown. * Significant difference *vs* healthy subjects $p<0.05$; ** Significant difference *vs* healthy subjects $p<0.001$.

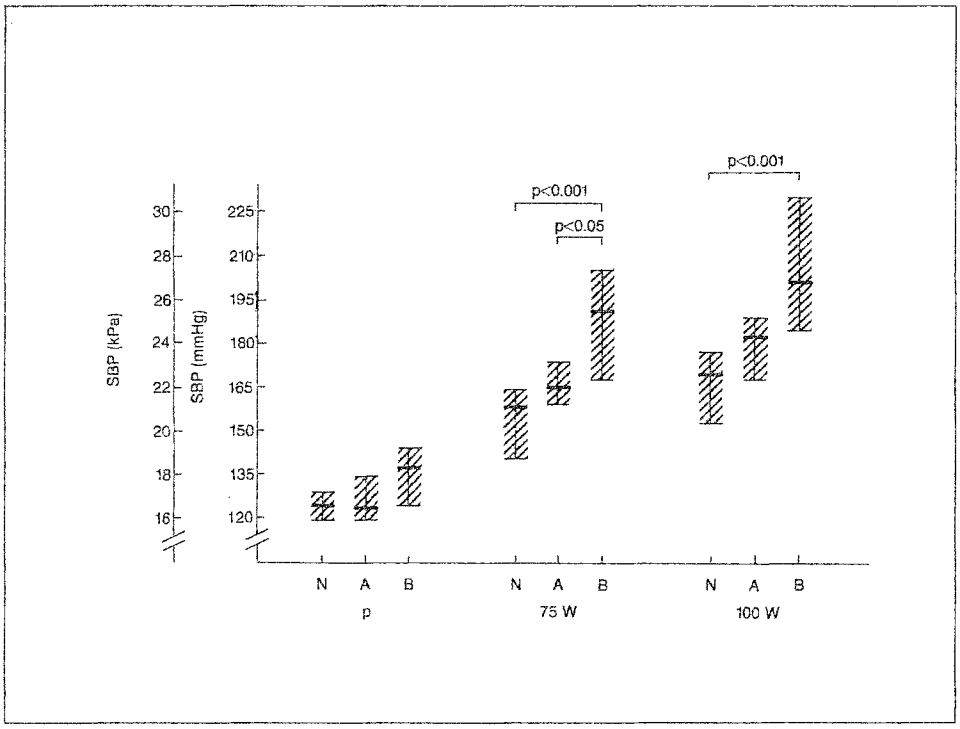


Fig. 1 - Systolic blood pressure (SBP) during pre-exercise resting period and 75 W and 100 W work loads in healthy subjects and in the two groups of diabetic patients. N = healthy subjects; A = diabetics with resting UAER≤16 μg/min; B = diabetics with resting 16 < UAER <126 μg/min. Periods: p = pre-exercise rest; 75 W and 100 W = work loads of 75 W and 100 W. Median and 95% confidence limits are shown.

confidence limits of regression coefficient: 0.9 - 3.2, $p<0.01$) and at the work load of 100 W ($r = 0.75$, regression equation: $\Delta UAER = 56.5 + 5.14$ UAER-p, 95% confidence limits of regression coefficient 1.48 - 8.8, $p<0.05$). Highest UAER was observed during the work load of either 75 W or 100 W in 11 Group A diabetic patients (58%) and in all 10 Group B diabetics. In the first post-exercise period, 7 Group A diabetic patients reached their highest values of UAER. However, these were almost identical with those at 100 W.

SBP and DBP increased significantly in all groups during the exercise test. A significant difference was found in SBP at the work load of 75 W between the two groups of diabetic patients ($p<0.05$) and between healthy subjects and Group B ($p<0.001$), but only between healthy subjects and Group B at the work load of 100 W ($p<0.001$) (fig. 1). Nine out of 10 Group B diabetics were found to have SBP equal to or exceeding 195 mmHg, whereas only 6 out of 19 Group A diabetics were found to have these values. A significant difference in DBP was found between healthy subjects and Group B patients at work loads of 75 W ($p<0.01$) and 100 W ($p<0.05$) (fig. 2).

There was no correlation between increase in SBP ($\Delta SBP$) and increase in UAER from resting to exercise values ($\Delta UAER$) in both groups of diabetic patients at 75 W and in Group B at 100 W. The only correlation between these

parameters was found in Group A at the work load of 100 W ($r = 0.53$, $\Delta UAER = -1.67 + 0.05 \cdot \Delta SBP$, $\Delta SBP = 49.59 + 6.16 \cdot \Delta UAER$, $p<0.05$).

Blood glucose did not change significantly in diabetic patients during the exercise test. The two groups did not differ in post-exercise blood glucose (tab. 4). We found no significant correlation between post-exercise blood glucose and UAER at 100 W in any of the groups examined.

## DISCUSSION

Physical exercise induces renal hemodynamic responses both in healthy subjects and in diabetic patients, namely a reduction in glomerular filtration rate, a more marked reduction in renal plasma flow and therefore an increase in filtration fraction. Diabetics with significant increase in UAER provoked by exercise test revealed a filtration fraction significantly higher compared to healthy subjects[30]. In another study, however, no difference in elevated filtration fraction during resting state and exercise between diabetic patients with normoalbuminuria and diabetics with microalbuminuria was found[9]. The increase in filtration fraction is mainly due to an increase in transcapillary hydraulic pressure in the glomeruli and therefore other factors determining permeability of the glomerular basement membrane (GBM) should be present. A decreased content of glycosaminoglycan heparane sulfate and sialic acid in GBM of diabetic humans and animals has been reported[6, 21, 32]. The hypothesis has been put forward that reduction in the anionic composition of the GBM is the primary event responsible for loss of its charge selective properties, leading to selective increase in urinary albumin excretion. This abnormality of

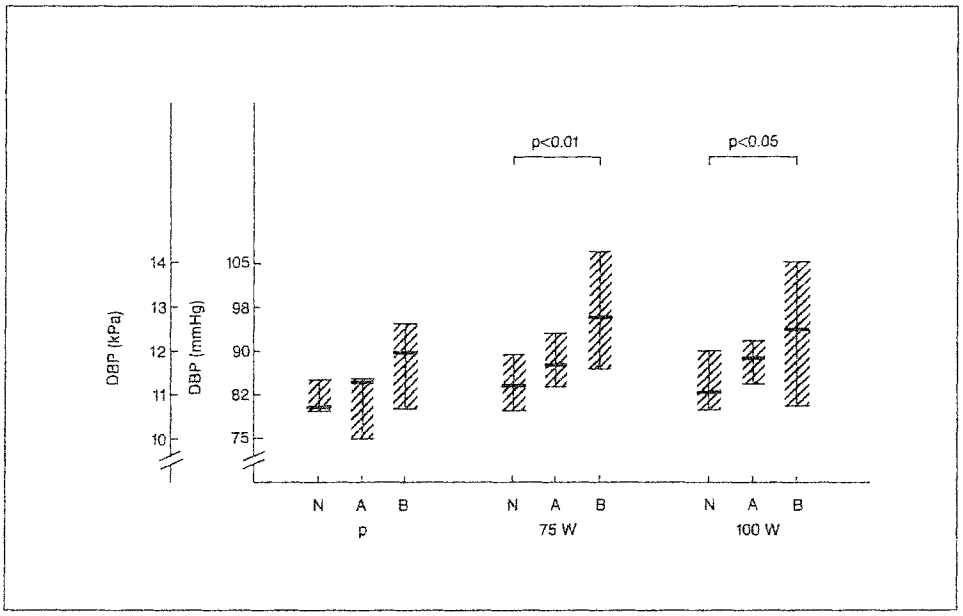


Fig. 2 - Diastolic blood pressure (DBP) during pre-exercise resting period and 75 W and 100 W work loads in healthy subjects and in the two groups of diabetic patients. For comments see fig. 1.

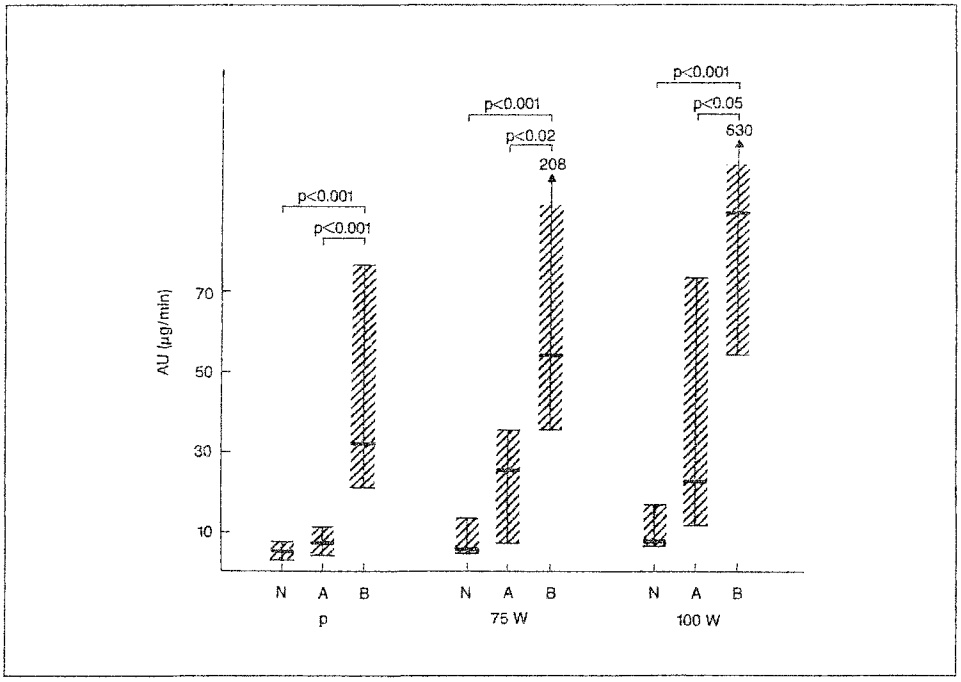


Fig. 3 - Urinary albumin excretion rate (AU) during pre-exercise resting period and 75 W and 100 W work loads in healthy subjects and in the two groups of diabetic patients. For details see fig. 1.

GBM is assumed to be independent of mesangial accumulation, GBM thickening and glomerular hemodynamics[8]. UAER reached the highest values almost in all our diabetics during the 100 W work load. Only few diabetic patients had their highest UAER in the first post-exercise resting period, the values being almost identical with those during exercise. In some previous studies, however, the highest UAER was observed mostly in the first post-exercise resting period or during the work load and subsequent resting period[27, 30]. This prolonged excretion of albumin is explained by a washing-out effect. The filtered albumin is probably retained in the tubular system during exercise-induced low urine output and then increasingly excreted as a result of a sudden rise in urine output at rest[28]. The difference in reported findings might be due to our modification of the test (urine collection in the second work load period was performed after a 5-min rest). It could be speculated that the elevation of albuminuria induced by exercise occurs mainly in the first 5 min of rest, in our study included in the work load period. We found considerably decreased UAER in the first post-exercise resting period, while UAER in the second post-exercise resting period was almost on the same level as before the test.

Healthy subjects increased their UAER during the exercise. The findings are consistent with the observations in adolescents[23], in adult men[9] and in athletes[13]. On the other hand, other authors did not find increased UAER in healthy teen-agers and adults during exercise[4, 7].

We observed the highest response of albuminuria to exercise in diabetic patients with elevated resting UAER - a fact that confirmed previous studies[4, 9].

It has been reported that there was no change in exercise-induced albuminuria in diabetic patients with basal normoalbuminuria with duration of diabetes under 2 years, whereas patients with longer duration of diabetes showed increased response of albuminuria[30]. Other authors found no difference in UAER during submaximal and maximal work load between diabetic and healthy children[3]. In our study, the difference in resting albuminuria between the diabetic groups decreased gradually depending on the work load performed. Thus, the values of exercise-induced albuminuria did not entirely correspond to the resting values. The interpretation of results in diabetic patients who 'did not keep the rules of their own group' (e.g. those with resting normoalbuminuria who exhibited high values of exercise-induced albuminuria) is not yet clear. This is still to be clarified by a longitudinal study of our patients.

Blood glucose did not significantly change during the exercise test, although a slight increase was observed in both groups of diabetic patients who were in a fasting state and did not receive their morning insulin dose. There was no correlation between blood glucose and UAER at the work load of 100 W in either group. From the literature, no correlation was found between actual blood glucose and UAER and between UAER and glycosuria in diabetic children[7]. On the other hand, short-term improvement of metabolic control decreased the albuminuric response to exercise in diabetic patients[7, 29, 31].

Diabetic patients and healthy subjects in our study did not differ in pre-exercise resting SBP and DBP and in mean SBP and DBP calculated from four previous outpatient measurements, which is in accordance with findings of another study[10]. In the study by WISEMAN et al.[33], there were significantly higher values of SBP and DBP in a high microalbuminuria group compared to a low microalbuminuria group and a control group, but the upper limit of albuminuria range in the former group was higher than in our Group B. The highest increase in SBP and DBP during exercise was observed in diabetic patients with microalbuminuria. However, no correlation between increase in SBP and increase in UAER could be found in the latter group of patients. Elevation of systemic blood pressure and increased transglomerular gradient do not seem to be the only factors determining the transport of albumin through the GBM. Disturbed metabolism of glucids is likely to have a profound effect on the change of filtration properties in the glomerulus[15].

The exercise test unmasked a higher reactivity of SBP and DBP during exercise in diabetic patients with microalbuminuria. In spite of the report that exercise-induced, abnormally raised SBP was not associated with later development of diabetic nephropathy[25], we consider it important to detect and follow diabetic and non-diabetic patients with exaggerated blood pressure reactivity to exercise as early as possible. These subjects are likely to develop fixed hypertension later on[2]. The early and effective treatment of hypertension is of crucial importance in reversing increased UAER and slowing down the progression of diabetic nephropathy[5, 22].

Our study showed lower working capacity of diabetic patients than that of comparable healthy subjects.

The appropriate amount of exercise that should be recommended to diabetic patients to increase their physical fitness must as yet be determined. We found exaggerated albuminuric response and hyperreactivity of blood pressure during exercise in diabetics with microalbuminuria. These are the factors

which in the long-term accelerate the progression of diabetic nephropathy. In accordance with a previous study[29], we suggest that the diabetic patient with microalbuminuria should use only less strenuous exercises in regular training and avoid regular training of the intensity performed in our study.

SUMMARY

Twenty-nine male type I diabetic patients (age range 16-46 years) and thirteen healthy men (age range 18-43 years) were exercised on a cycling ergometer at 75 W and 100 W after having achieved a steady state of water diuresis. Diabetic patients were subdivided into Group A ($n = 19$, resting urinary albumin excretion rate - UAER $\leq 16$ μg/min) and Group B ($n = 10$, $16 <$ resting UAER$<126$ μg/min). The groups were comparable in weight, serum creatinine, duration of diabetes and glycosylated hemoglobin. Group B showed the highest elevation of UAER at the work load of 100 W, with no correlation between increase in UAER and increase in systolic blood pressure (SBP) at both work loads. The only correlation between these parameters was found in Group A at the work load of 100 W ($p<0.05$). No correlation was found between exercise UAER and actual blood glucose in either group. The difference in UAER between healthy subjects and Group B patients ($p<0.001$) remained on the same level during exercise as at rest, but the difference between Group A and Group B ($p<0.001$) decreased with increasing work load ($p<0.05$). The highest exercise-induced systolic and diastolic blood pressure (DBP) was found in Group B, although there was no difference between the diabetic groups in pre-exercise blood pressure and in mean SBP and DBP from previous outpatient check-ups. Blood glucose did not change significantly during exercise in either diabetic group. Working capacity of diabetic patients was lower than that of healthy subjects. The test revealed some diabetic patients with strong elevation of UAER and with abnormally raised systolic and diastolic BP during exercise. The value of the findings reported is to be clarified in a further longitudinal study.

REFERENCES

1. Andersen A. R., Christiansen J. S., Andersen J. K., Kreiner S., Deckert T.: Diabetic nephropathy in type 1 (insulin-dependent) diabetes: an epidemiological study - Diabetologia *25*, 496, 1983.
2. Benbassat J., Froom P.: Blood pressure response to exercise as a predictor of hypertension - Arch. intern. Med. *146*, 2053, 1986.
3. Brouhard B. H., Allen K., Sapire D., Travis L. B.: Effect of exercise on urinary N-acetyl-beta-D-glucosaminidase activity and albumin excretion in children with type I diabetes mellitus - Diabet. Care *8*, 466, 1985.
4. Christensen C. K.: Abnormal albuminuria and blood pressure rise in incipient diabetic nephropathy induced by exercise - Kidney int. *25*, 819, 1984.
5. Christensen C. K., Mogensen C. E.: Correlations between blood pressure and kidney function in insulin-dependent diabetics: with emphasis on incipient nephropathy - Diabet. Nephropathy *4*, 34, 1985.
6. Cohen M. P., Surma M. L.: Effect of diabetes on *in vivo* metabolism of [$^{35}$S]-labeled glomerular basement membrane - Diabetes *33*, 8, 1984.
7. Dahlquist G., Aperia A., Carlsson L., Linné T., Persson B., Thorén C., Wilton P.: Effect of metabolic control and duration on exercise-induced albuminuria in diabetic teen-agers - Acta paediatr. scand. *72*, 895, 1983.
8. Deckert T., Feldt-Rasmussen B., Mathiesen E., Baker L.: Pathogenesis of incipient nephropathy: a hypothesis - Diabet. Nephropathy *3*, 83, 1984.
9. Feldt-Rasmussen B., Baker L., Deckert T.: Exercise as a provocative test in early renal disease in type 1 (insulin-dependent) diabetes: albuminuric, systemic and renal haemodynamic responses - Diabetologia *28*, 389, 1985.

10. Feldt-Rasmussen B., Mathiesen E. R., Deckert T., Giese J., Christensen N. J., Bent-Hansen L., Nielsen M. D.: Central role for sodium in the pathogenesis of blood pressure changes independent of angiotensin, aldosterone and catecholamines in type 1 (insulin-dependent) diabetes mellitus - Diabetologia *30*, 610, 1987.

11. Hermansson G., Ludvigsson J.: Renal function and blood pressure reaction during exercise in diabetic and non-diabetic children and adolescents - Acta paediatr. scand. (Suppl.) *283*, 86, 1980.

12. Hirose K., Shinozoku M., Yajima Y.: Diabetic nephropathy. in Japan. In: Abe H., Hoshi M. (Eds): Diabetic microangiopathy Japan Medical Research Foundation Publication nº 20. University of Tokyo Press, Tokyo, 1983; p. 81.

13. Houser M. T.: Characterization of recumbent, ambulatory and postexercise proteinuria in the adolescent - Pediatr. Res. *21*, 442, 1987.

14. Huttunen N.-P., Kaar M.-L., Puukka R., Åkerblom H. K.: Exercise-induced proteinuria in children and adolescents with type 1 (insulin-dependent) diabetes - Diabetologia *21*, 495, 1981.

15. Laurell C. B.: Quantitative estimation of proteins by electrophoresis in agarose gel containing antibodies - Analyt. Biochem. *15*, 45, 1966.

16. Mauer S. M., Steffes M. V., Goetz F. C., Sutherland D. E. R., Brown D. M.: Diabetic nephropathy. A perspective - Diabetes *32* (Suppl. 2), 52, 1983.

17. Mikulecký M.: Základy biometriky pre experimentálnu a klinickú medicínu - Univerzita Komenského, Bratislava, 1985.

18. Mogensen C. E.: Diabetes mellitus and the kidney - Kidney int. *21*, 673, 1982.

19. Mogensen C. E., Christensen C. K.: Predicting diabetic nephropathy in insulin-dependent patients - New Engl. J. Med. *311*, 89, 1984.

20. Mogensen C. E., Vittinghus E., Solling K.: Abnormal albumin excretion after two provocative renal tests in diabetes: physical exercise and lysine injection - Kidney int. *16*, 385, 1979.

21. Parthasarathy N., Spiro R. G.: Effect of diabetes on the glycosaminoglycan component of the human glomerular basement membrane - Diabetes *31*, 738, 1982.

22. Parving H.-H., Andersen A. R., Smidt U. M.: The effect of long-term antihypertensive treatment on kidney function and albuminuria in diabetic nephropathy - Diabet. Nephropathy *4*, 52, 1985.

23. Poortsmans J., Dorchy H., Toussaint D.: Urinary excretion of total proteins, albumin and $\beta_2$-microglobulin during rest and exercise in diabetic adolescents with and without retinopathy - Diabet. Care *5*, 617, 1982.

24. Sheffield L. T., Holt J. H., Reeves T. J.: Exercise graded by heart rate in electrocardiography for angina pectoris - Circulation *32*, 622, 1965.

25. Torffvit O., Persson G.: Is exercise-induced blood pressure rise predictive of nephropathy in insulin-dependent diabetes? - Acta med. scand. *221*, 299, 1987.

26. Viberti G. C., Hill R. D., Jarrett R. J., Argyropoulos A., Mahmud U., Keen H.: Micro-albuminuria as a predictor of clinical nephropathy in insulin-dependent diabetes mellitus - Lancet *i*, 1430, 1982.

27. Viberti G. C., Jarrett R. J., McCartney M., Keen H.: Increased glomerular permeability to albumin induced by exercise in diabetic subjects - Diabetologia *14*, 293, 1978.

28. Viberti G. C., Mogensen C. E., Keen H., Jacobsen F. K., Jarrett R. J., Christensen C. K.: Urinary excretion of albumin in normal man: the effect of water loading - Scand. J. clin. Lab. Invest. *42*, 147, 1982.

29. Viberti G. C., Pickup J. C., Bilous R. W., Keen H., Mackintosh D.: Correction of exercise-induced microalbuminuria in insulin-dependent diabetics after 3 weeks of subcutaneous insulin infusion - Diabetes *30*, 818, 1981.

30. Vittinghus E., Mogensen C. E.: Albumin excretion and renal hemodynamic response to physical exercise in normal and diabetic man - Scand. J. clin. Lab. Invest. *41*, 627, 1981.

31. VITTINGHUS E., MOGENSEN C. E.: Graded exercise and protein excretion in diabetic man and the effect of insulin treatment - Kidney int. *21*, 725, 1982.

32. WAHL P., DEPPERMANN D., HASSLACHER CH.: Biochemistry of glomerular basement membrane of the normal and diabetic human - Kidney int. *21*, 744, 1982.

33. WISEMAN M., VIBERTI G. C., MACKINTOSH D., JARRETT R. J., KEEN H.: Glycaemia, arterial pressure and micro-albuminuria in type 1 (insulin-dependent) diabetes mellitus - Diabetologia *26*, 401, 1984.

*Requests for reprints should be addressed to:*

PETER PONŤUCH
*I. interná klinika - Fakultná nemocnica*
*Mickiewiczova ul. c. 13*
*813 69 Bratislava - Czechoslovakia*