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CREATININE CLEARANCE AND 24-HOUR CREATININE EXCRETION PROFILE IN THE URINE OF PEOPLE AFTER PHYSICAL EXERCISES

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Abstract. Physical exercise is one of the factors disturbing organism homeostasis which can be seen in the urine composition owing to the changes in the hemodynamic and metabolic processes in the kidneys. The aim of the study was the evaluation of the influence of physical exercise on the blood serum and urine creatinine concentration in the 24-h urine collection and on creatinine clearance. The study was also to prove the applicability of creatinine concentration in the urine as a reference parameter for other biochemical indices determined in the post-exercise urine. The group under study comprised 7 students. The 24-h urine collection was carried out in the group of students twice with an interval of three weeks. During the first 24-h collection (test 1) students performed the progressive test on the cycloergometer. The second 24-hour collection (test 2) was taken during a routine physical activity and the subjects were free of strain. The material for the tests was the urine collected during 24 h and the blood collected from the vein three times in test 1: pre-exercise, immediately after the exercise and after 24 h in test 2 - once in the morning on the completion of the urine collection. The urine creatinine was determined by means of the colorimetric method, the serum creatinine concentration was determined in a biochemical analyzer BioMèrieux. In the blood taken after exercise and at rest the lactate concentration was estimated by the Dr Lange test. Endogenic creatinine clearance (ml/min/1.73 m^2 body surface) was also calculated. The differences in creatinine concentrations in the urine in the test with exercise were only by 7.7% higher and were negligible. However, creatinine concentration in the blood serum in the same test was by 13 per cent higher and this difference was at the significance level $p \leq 0.05$. Creatinine concentration increase in the serum was due to post-exercise reduction in plasma volume (%ΔPV=—11.75%±4.77). Also the 24-h urination was similar in both tests. Creatinine clearance values expressed in ml per min per 1.73m^2 of body surface are lower in test 1 (exercise) than creatinine clearance values in test 2 (at rest); individual differences do not exceed 9%. With the obtained results, it can be said that a moderate physical effort does not disturb the filtration function of glomerula,

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nor does it affect creatinine excretion, which makes this parameter suitable for expressing the activity of the examined enzymes, proteins and other biochemical parameters determined in the post-exercise urine. This coefficient eliminates mistakenly interpreted increases in biochemical indices owing to dehydration and the decrease in the volume of the passed urine.

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Key words: Creatinine clearance – Exercise - Progressive test - Urine

Introduction

The kidneys play an important role in maintaining the homeostasis of an organism due to their regulation, endocrine, metabolic and excretory functions. The regulation function retains the hydro-electrolyte and acid-alkaline balance. The endocrine function is connected with producing such hormones as renin (an enzyme of hormone-like qualities), angiotensin II, prostaglandins and leucotrenes, erythropoietin and with activating calcidiol (25-hydroxyvitamin D) to calcitriol (1.25-dihydroxyvitamin D3) [1,3]. The metabolic function needs the kidneys for carbohydrate metabolism, carnitine and creatine biosynthesis and degradation of numerous hormones, medicines and toxins. Thanks to the excretory function, the final metabolic products like urea, creatinine, uric acid, sulphates and phosphates are removed.

All these processes result in preserving the stability of chemical composition and the volume of extracellular fluid and blood pressure. Through kidneys pass 1000-1200 ml of blood per min which corresponds to 20-25% of stroke volume. From this volume 120 ml of plasma/min is filtrated in glomerules of normal kidneys, which value is called GFR - glomerular filtration rate. This is the basic mechanism of urine production. The final composition of the urine is the result of the glomerular filtration processes, as well as of absorption, secretion and nephron tubular diffusion. The urine samples are obtained in a non-invasive way, which makes it a useful diagnostic material for many biochemical tests applied in physiological and pathological states [4,10,17]. Physical exercise is one of the factors disturbing organism homeostasis which can be seen in the urine composition owing to the changes in the hemodynamic and metabolic processes in the kidneys. Further effects are post-exercise proteinuria and enzymuria as well as the increased secretion of other compounds like hormones, metabolites and electrolytes [4,14]. In physiological states, with the regular filtration-reabsorption functions of the kidneys, proteins and enzymes present in the urine originate partly from renal cells and partly from filtration of the plasma and from the urinary tract.

Physical strain limits blood flow through the kidneys and enhances its pressure [19]. Simultaneously, the concentration of hydrogen cations and the CO_2 partial pressure grow, and ATP falls down. These changes may disturb the glomerular filtration and reabsorption mechanisms, which in turn alter the chemical composition of the post-exercise urine.

The increase or decrease in the enzyme activity and in the concentration of various proteins in the urine can either reflect changes within the kidney itself or can be due to extra-renal reasons. The determination of the enzyme activity and protein concentrations in the urine is a non-invasive and sensitive method of detecting early changes in the kidneys in the situation when all traditional indices of kidney functioning remain normal [10]. In clinical studies the so-called 24-h urine collection is commonly employed. The patient's urine is collected during 24 h in one container and the components under study are expressed against a 24-h urine collection. However, this method should not be applied in screening post-exercise changes, as the majority of the studied parameters reveal changes in time in excreting after the strain and are back to normal values during the following 24 h [4]. In order to observe post-exercise changes in biochemical parameters in the urine, they are evaluated in single specimens. In diagnostics various methods for determining concentrations or activities of the urine parameters are used because of the changes in the volume of the urine voided. They can be expressed as a ratio to the urine volume, time and creatinine concentration [12]. The above method is the most popular one [2], although it is being criticized for the correspondence of the creatinine excreted during 24 h to various factors: age, sex, body mass, diet and the presence of other chromogenic substances in the urine interfering with creatinine in the methods used for its evaluation [23]. Creatinine is creatine anhydride produced during nonenzymatic dehydration of phosphocreatine [7]. Daily ca 1-2% of muscle phosphocreatine is degraded to creatinine [7]. Creatinine has been found useful in kidney diagnostics because it is excreted from the organism only by the kidneys. In physiological states, it is neither reabsorbed nor actively secreted in renal tubules. Its concentration in the blood serum correlates negatively with GFR and this makes it a useful index for the kidney filtration function [3].

One of the tests examining the kidney functions is the measurement of glomerular filtration in respect of the clearance of endogenic creatinine, i.e. the ability of removing it and excreting by the kidneys. The value of creatinine clearance depends on nephron functioning and in healthy subjects on age, body mass, and also the dietary supply of proteins, salt and water and physical effort.

The aim of the study was the evaluation of the influence of physical exercise on the blood serum and urine creatinine concentration in the 24-h urine collection and on creatinine clearance. The study was also to prove the applicability of creatinine concentration in the urine as a reference parameter for other biochemical indices determined in the post-exercise urine.

Materials and Methods

The group under study comprised 7 students in the second year of The University School of Physical Education in Wrocław who do not take sports professionally. The group description is given in Table 1. The 24-h urine collection was carried out in the group of students twice with an interval of three weeks.

During the first 24-h collection (test 1) students performed the progressive test on the cycloergometer Monark 839 E (Sweden) with an optical sensor which makes it possible to accurately measure work in kJ. The test was performed with an initial load of 10 N increasing every 3 min by 10 N with the frequency over 60 rpm until the subject refused to perform the test. Oxygen consumption was measured using ERGO – Oxyscreen (Jaeger Germany).

The second 24-h collection (test 2) was taken during a routine physical activity and the subjects were free of strain. All the subjects on the day prior to the tests did not perform any strenuous work and before and during the examinations they did not take medicines and their daily intake of meat did not exceed 300 grams.

The material for the tests was the urine collected during 24 h and the blood collected from the vein three times in test 1:
A - pre-exercise, B - immediately after the exercise, C - after 24 h in test 2 - once in the morning on the completion of the urine collection.

The urine collection followed laboratory procedures and began in the morning with the second specimen of the urine and finished with the first specimen the following day. Each specimen voided by the subject during 24 h was collected in a separate container and was measured for volume and density. The urine was then centrifuged at +4 ^{0}C 3000·g and the supernatant underwent further biochemical tests and the sediment was examined with a light microscope. From each urine specimen 1ml was taken to evaluate the concentration of creatinine in a 24-h collection. The urine creatinine was determined by means of the colorimetric method with picric acid with the Biochemtest Kreatynina MPK POCH Gliwice kite; the serum creatinine concentration was determined in a biochemical analyzer BioMèrieux (France). In the blood taken from a finger tip after exercise and at rest the lactate concentration was estimated by the Dr Lange test. Endogenic creatinine clearance (ml/min/1.73 m^2 body surface) was calculated from the formula [7]:

$$CL_{creatinine} = \frac{U \times V}{P} \times \frac{1}{t} \times \frac{1.73}{A}$$

U- urine creatinine concentration (24-h collection) (mg/dl)
V - 24-h volume of urine (ml)
P - blood serum creatinine concentration (mg/dl)
A - body surface (m^2)
t - time of urine collection (min)

Hemoglobin (Hb), hematocrit (Hct) and red blood cell (RBC) count were measured an automatic analyzer ABX Micros analyzer (France).

Percentage change in plasma volume (%ΔPV) was calculated from pre- and post-exercise value of Hb and Hct according to the equation by Strauss [24].

The results were analysed statistically and were determined by means of Student-t test and Pearson's correlation coefficient.

Results

Table 1
Characteristics of the group under study and physiological parameters gained in progressive test

No	age (years)	body mass (kg)	body height (cm)	$VO_{2\,max}$ (ml /kg/min)	work (k J)	HR cycle/min	Lac mmol/l
1.	21	70	178	44.9	181.5	173	12.8
2.	21	82	187	46.9	178.3	212	13.1
3.	21	65.5	175	54	173.1	180	12.3
4.	21	72	179	54.8	191.7	182	11.5
5.	20	69.5	176	54.1	171.4	201	14.6
6.	21	68,5	171	49.4	171	199	12
7.	21	86	185	44.8	162.8	177	10.8
x	20.86	73.64	178.71	49.84	175.69	189.14	12.44
±	0.35	6.76	5.20	4.12	8.54	13.64	1.13

Table 1 shows the characteristics of the subjects. The group was homogeneous in respect of age, and the remaining parameters like body mass and height were similar. The subjects' VO_2max values in the progressive test were 49.84±4.12 $ml \cdot kg^{-1} \cdot min^{-1}$ and they correspond to average values obtained by males in this age group [25].

Table 2 gives creatinine concentrations in the 24-h collection of urine in test 1 (exercise) and test 2 (rest). The differences in creatinine concentrations in the urine in the test with exercise were only by 7.7 per cent higher and were negligible. However, creatinine concentration in the blood serum in the same test was by 13 per cent higher and this difference was at the significance level $p \le 0.05$. Post-exercise changes were observed in selected hematological parameters; the Ht value, Hb concentration and RBC number increased by 7% after the exercise when compared to the parameter values prior to exercise ($p \le 0.001$).

Similarly, percentage change in plasma volume (%Δ PV) calculated from these parameters ranged from – 5.99 % to –20.33% (mean – 11.75%±4.77), and after 24 h were close to values at rest (Table 3).

The 24-h urination was similar in both tests.

Table 2
Urine creatinine concentrations in a 24-h collection, serum creatinine concentration and creatinine clearance

exerc. /rest	24-h urine volume V (ml)		urine creatinine (mg/dl)		serum creatinine (mg/dl)		creatinine clearance ($ml/min/1.73m^2$)	
No	exerc.	rest	exerc.	rest	exerc.	rest	exerc.	rest
1	1160	806	167.86	182.06	1.05	0.90	139.0	143.28
2	1382	1370	150.00	150.00	1.16	1.03	107.68	146.43
3	1048	769	175.00	196.43	1.04	0.89	141.02	143.65
4	1631	1789	132.14	108.6	1.00	0.92	155.26	167.19
5	1302	1316	139.29	106.00	1.07	0.85	132.26	142.70
6	1178	1259	160.71	122.14	1.03	0.90	126.8	136.28
7	1223	1107	178.57	163.57	1.13	1.05	120.51	132.15
x	1274.86	1187.14	157.65	147.09	1.07**	0.93	131.79*	144.53
±	±175.57	±344.59	±16.47	±33.35	±0.05	±0.07	±14.25	±10.31

*p≤0.005, **p≤0.05

Table 3
Changes in hematological parameters: hemoglobin (Hb) concentration, hematocrit (Hct), red blood cell (RBC) and percent change in plasma volume (%Δ PV) in pre- and post- and 24 h post-exercise

	Hb g/dl			Hct %			RBC T/l			%Δ PV	
No	pre-	post-	24 h post-	pre-	po-	24 h post-	pre-	post-	24 h post-	post-	24 h post-
1	17.0	17.3	16.0	49.3	51.5	50.0	5.27	5.54	5.22	-5.99	+4.78
2	15.4	16.7	15.8	47.9	50.3	47.0	5.23	5.64	5.28	-12.03	-0.85
3	12.3	13.3	12.9	38.9	42.2	39.6	4.57	4.90	4.69	-12.51	-5.74
4	14.8	15.6	15.1	44.3	47.4	45.6	5.25	5.58	5.34	-10.41	-4.28
5	15.5	16.5	15.2	46.4	50.9	44.8	5.21	5.6	5.03	-13.95	+5.01
6	14.2	15.7	15.3	40.4	47.5	45.4	4.76	5.55	5.30	-20.33	-14.98
7	14.4	15.1	14.0	43.5	44.9	42.1	5.03	5.19	4.88	-7.00	+5.41
x	14.76	15.74*	14.9	44.39	47.81*	44.93	5.05	5.43*	5.11	-11.75*	-1.52
±	1.47	1.31	1.09	3.82	3.41	3.34	0.28	0.28	0.25	4.77	7.50

*$p \leq 0.001$

Figs. 1-7 demonstrate individual profiles of the 24-h creatinine excretion in urine in tests 1 and 2. On the charts the hour of the performance of the progressive test is marked. The charts show a high individual variability in creatinine excretion depending on the time of the day. Also post-exercise changes in creatinine concentration were not the same - in subjects 1 and 2 in the urine voided immediately after the exercise, the creatinine concentration increase was threefold and then decreased, and the following increase was observed 12 hours after the performance of the test. However, a 24-h profile of creatinine changes in the same subjects in the urine collected without the exercise (test 2) is similar to the results in the exercise test (Figs. 1 and 2).

In the remaining subjects effort diminishes creatinine concentration in the first urine specimen collected after the test and these tendencies are in line with the 24-h changes in the urine collected without the exercise test (Figs. 3-7).

Creatinine clearance values expressed in ml per min per 1.73m^2 of body surface are given in Table 2. It was shown that they are lower in test 1 (exercise) than creatinine clearance values in test 2 (at rest); individual differences do not exceed 9% except for subject 2 in whom the difference is 26%.

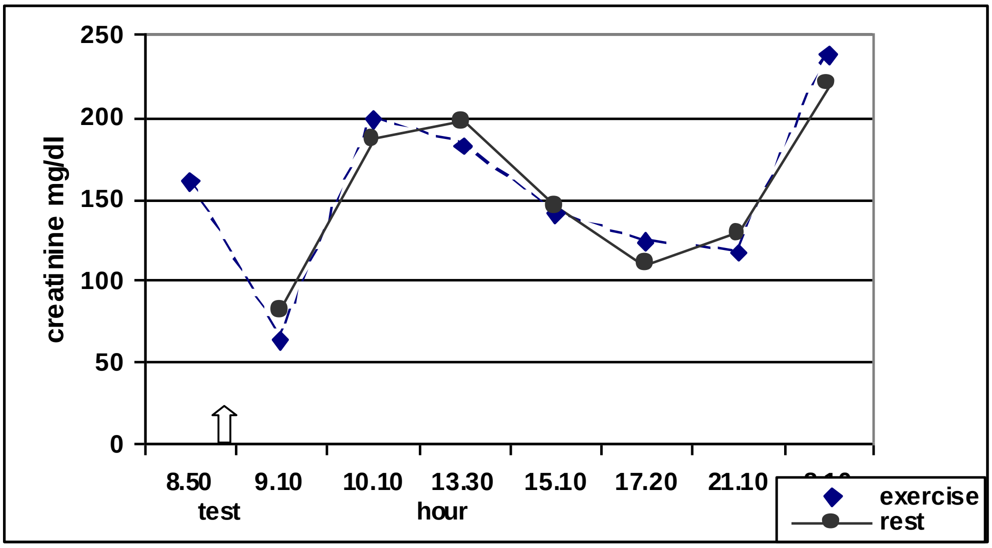

Fig. 1
24-h creatinine excretion profile in the urine of subject 1

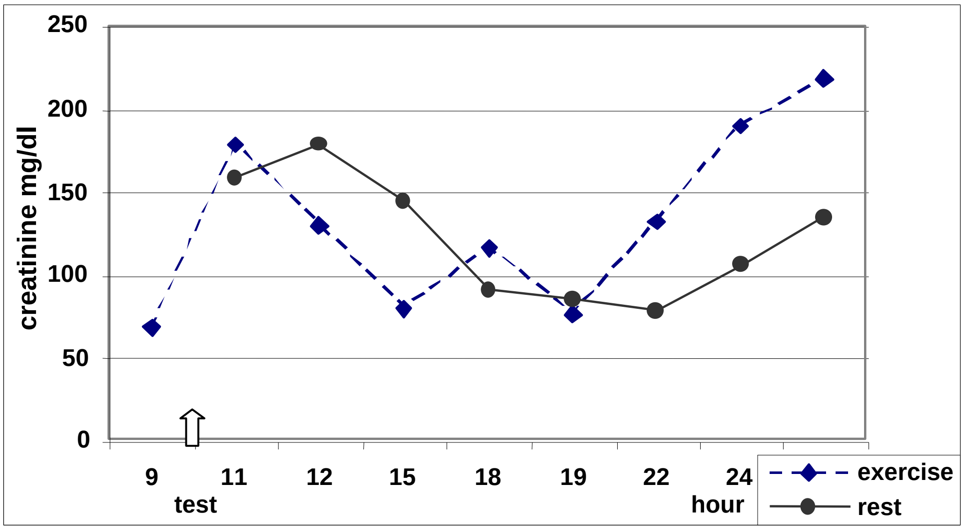

Fig. 2
24-h creatinine excretion profile in the urine of subject 2

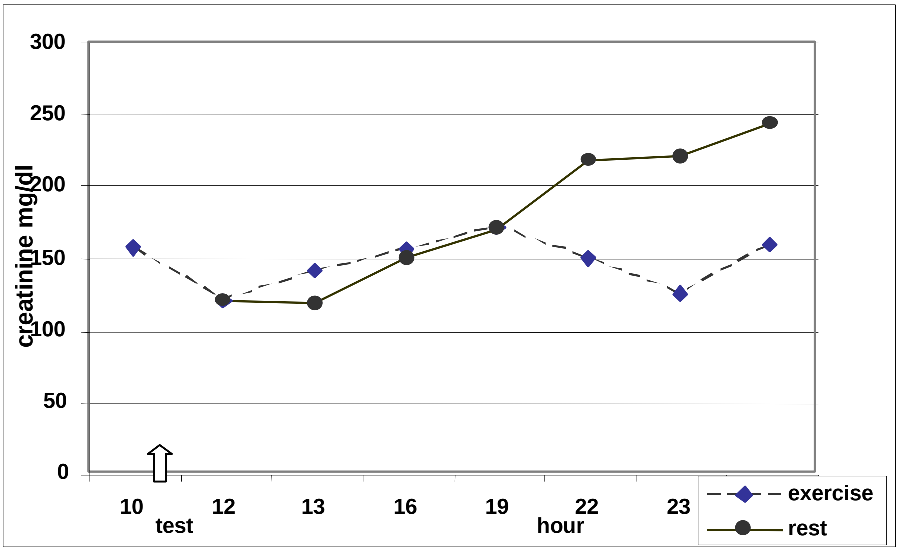

Fig. 3
24-h creatinine excretion profile in the urine of subject 3

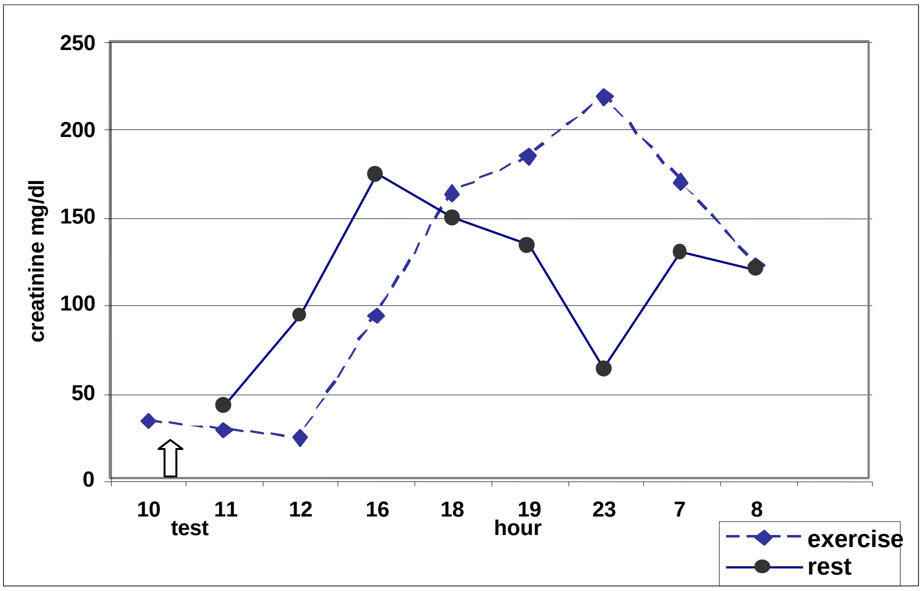

Fig. 4
24-h creatinine excretion profile in urine of subject 4

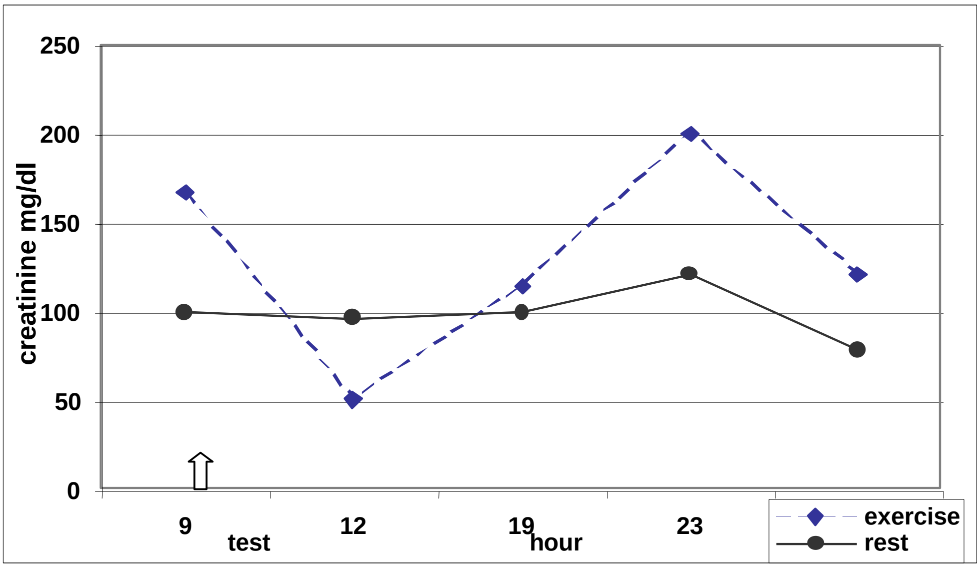

Fig. 5
24-h creatinine excretion profile in the urine of subject 5

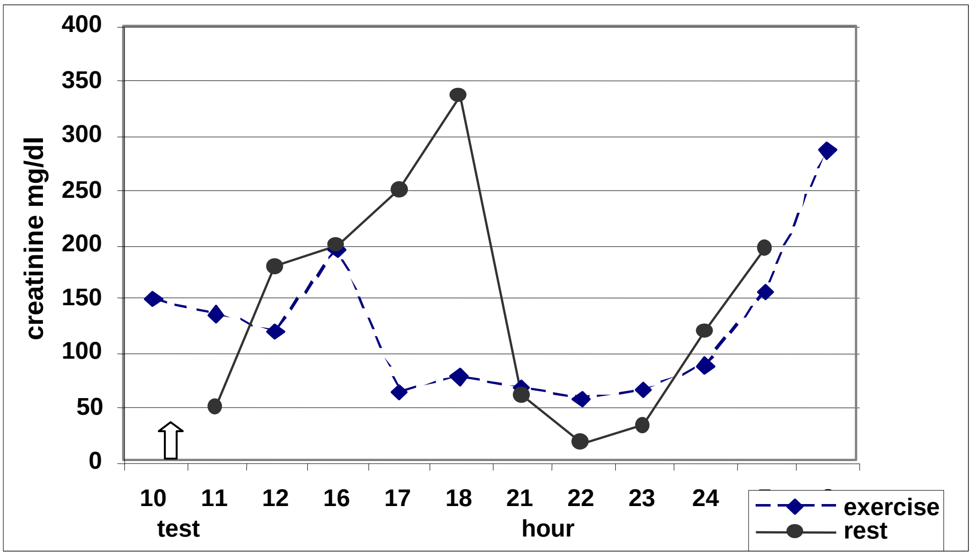

Fig. 6
24-h creatinine excretion profile in the urine of subject 6

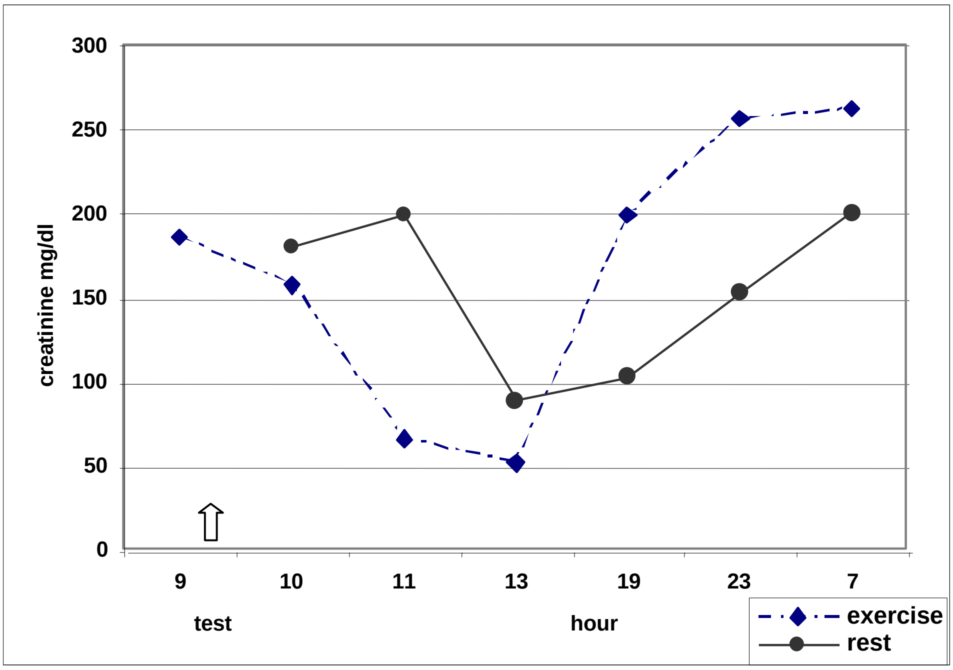

Fig. 7
24-h creatinine excretion profile in the urine of subject 7

The calculated correlation coefficients showed in test 1 the following ratios: VO_2max/creatinine in the urine r=-0.563; VO_2max/creatinine in the blood serum r=-0.461; VO_2max/creatinine clearance r=0.611; creatinine clearance/work r=0.584 and urine creatinine/lactate r=-0.421. These coefficients were not statistically significant.

Discussion

Physical exercise changes the organism homeostasis. There are reports on the effect of the kind of physical effort, load, time of its duration and the position of the performed task on the volume and composition of body fluids [15,21].

It was shown that strenuous exercise performed in the upright and supine postures causes a similar reduction in plasma volume immediately after the performance, whilst 22 h later the plasma volume increased by 6.5% in the subjects performing the exercise in the upright posture and decreased by 3.4% in those performing in the supine posture.

The same pattern of loads decreased creatinine clearance (ml/min) in the task performed with upright posture by 20% which attained the values of the control group within 2 h and the second group revealed no differences [15]. Different ways of calculating creatinine clearance result in various values of this parameter quoted in literature. According to some authors, correct values range from 129.3±55.3 ml/min/1.73m^2 [6], others hold that the values are - 140±3.7 ml/min/ 1.73m^2 [3]. In clinical studies a simplified way of expressing clearance in ml per min is used, yet it ignores the differences in body mass and in muscle mass in particular, and yet it is muscle mass that is the source of as much as 98% of the blood serum creatinine [18]. The factor affecting the clearance value is age and it was proved that this parameter increases until the age of 20-25 years and then decreases by 10 ml per min with each decade of life [3,9]. For each age group under study, the values of creatinine clearance range is 140±3.7 ml/min/1.73 m^2. Creatinine clearance values gained in the test at rest fell within the normal range and were 144.53±10.31 ml/min/1.73 m^2 except subject 4 in whom the clearance value was 167.19 ml/min/1.73 m^2. In the exercise test the clearance values were 9 per cent lower than the clearance values in the test at rest and were 131.79±14.25 ml/min/1.73m^2 and in subject 4 it was 155.26 ml/min/1.73 m^2. A slight decrease in creatinine clearance value as the result of GFR drop is connected with a limited blood flow through the kidneys owing to the catecholamine influence on afferent arteriole and the secretion of vasopressin [14]. However, such negligible changes do not testify to the impairment of the glomerular filtration function [17]. In pathological states these differences exceed correct values by at least 10 per cent. In Poortmans' studies [20] in the group of people aged 20-30 years performing the progressive test on a cycloergometer (50%VO_2max) creatinine clearance expressed in ml/min was 110±7 prior to exercise and after the exercise it fell down to 79±17 ml per min. Such a significant lowering of clearance was connected with the short time of urine collection which was 90 min.

In these studies an increase in creatinine concentration was observed in the blood serum from 0.93±0.07 mg per dl at rest to 1.07±0.05 mg per dl in the exercise test ($p \leq 0.005$).

Creatinine concentration increase in the serum was due to post-exercise reduction in plasma volume. Percentage change in plasma volume (%Δ PV) calculated from pre-, post-exercise Hb and Hct, ranged from – 5.99 % to –20.33% (mean – 11.75%±4.77), and after 24 h were close to values at rest. A similar decrease (-20%) was reported by Rotstein *et al.* [22] in subjects investigated during the effort in different environmental conditions.

Also the urine creatinine concentration was higher in exercise test by 7% and this difference is not statistically significant. These results are close to the post-exercise values obtained by other researchers [15,21]. Observations of the 24-h creatinine excretion show a high individual variability which is retained both in the exercise test and at rest in a given subject. According to Orłowski [17], creatinine excretion is the highest during daily activities and the lowest at night. These studies have not confirmed explicitly this relationship.

With the obtained results, it can be said that a moderate physical effort does not disturb the filtration function of glomerula (GFR), nor does it affect creatinine excretion, which makes this parameter suitable for expressing the activity of the examined enzymes, proteins and other biochemical parameters determined in the post-exercise urine [5,11,19]. This coefficient eliminates mistakenly interpreted increases in biochemical indices owing to dehydration and the decrease in the volume of the passed urine [8,16].

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