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CLIN. CHEM. 34/12, 2516–2518 (1988)

Influence of Strenuous Exercise on Albumin Excretion

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Renal albumin excretion rate was 7.3 mg/24 h (SEM 0.5, range 0.6–21.0) in 66 healthy subjects. This rate increased markedly during and shortly after strenuous exercise on a bicycle ergometer (before: 5.5 ± 0.6 μg/min; during and just after: 16.9 ± 2.2 μg/min; $P < 0.001$; n = 30). However, albumin excretion/24 h was not significantly higher during 24 h with a period of strenuous exercise than during 24 h without such exercise (10.3 ± 0.9 mg/24 h vs 8.5 ± 0.7 mg/24 h).

Additional Keyphrases: *albuminuria · diabetes · diabetic nephropathy*

End-stage renal disease develops in about 40% of insulin-dependent diabetics (*1, 2*), overt proteinuria (>500 mg of protein or >300 mg of albumin excreted in 24 h) being the hallmark of diabetic nephropathy and a serious prognostic marker (*1–3*). Pauci("micro")albuminuria is a strong predictor of future overt nephropathy (*4, 5*) in diabetic patients. Early paucialbuminuria can be stopped or even reversed by means of better control of blood glucose or of blood pressure (*3, 6, 7*), thus probably slowing or even preventing development of overt diabetic nephropathy. Exact estimation of a slight albuminuria is also of interest for the control of patients with hypertension (*8*). Our aim in this study was to examine whether 24-h albumin excretion is altered misleadingly by a rather brief period of strenuous exercise during the urine-collection period.

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Received July 11, 1988; accepted September 9, 1988.

Materials and Methods

Urinary albumin was measured by enzyme-linked immunosorbent assay as described previously (*9*). Urine samples were collected in 2-L casein-coated polyethylene containers (*9*). Albumin excretion was measured in 24-h collections of urine from 66 apparently healthy subjects (eight men and 10 women, ages 20–29 y; 10 men and 10 women, ages 30–39 y; eight men and 10 women, ages 40–49 y; and five men and five women, ages 50–55 y). In 30 of those subjects (five of each sex in the age ranges 20–29, 30–39, and 40–50 y) the 24-h collections were made as two 12-h collections (one from 0700 to 1900 hours, the second overnight from 1900 to 0700 hours) to contrast night-time with daytime excretion. With the same 30 subjects, we estimated albumin excretion rate before (period I), during and shortly after (period II), and after (period III) strenuous exercise. Period I lasted from 0700 to the start of the exercise, period II from the start of the exercise until 1 h after the end of the exercise, and period III from 1 h after the exercise until 0700 hours on the next day.

Results from periods I, II, and III were pooled to provide a 24-h period including exercise, which could then be compared with a 24-h period without exercise in the same subject. The two 24-h urine collections were done within one week, but not on consecutive days. The subjects performed strenuous exercise on a bicycle ergometer (Keiper Dynavit; Meditronic 40/2, 6750 Kaiserslautern, F.R.G.), according to the following protocol: Start with a workload of 30 W (J/s, or $kg \cdot m^2 \cdot s^{-3}$) for 3 min and increase to 70 W for 3 min, then further increase the workload by 40 W every 3 min until physical exhaustion. Blood pressure was measured with a sphygmomanometer. A statistical evaluation was by means of paired *t*-test; data are reported as mean ± SEM.

Results

For the 66 healthy subjects, the mean 24-h albumin excretion was 7.3 ± 0.5 mg/24 h (range 0.6–21.0), being 7.8 ± 0.8 (2.0–21.0) mg/24 h for the women and 6.7 ± 0.7 (0.6–19.5) mg/24 h for the men. The 12-h albumin excretion was significantly higher ($P < 0.05$) during day (4.9 ± 0.6 mg/12 h) than night (3.6 ± 0.3 mg/24 h) in 30 of those healthy controls. Albumin excretions per 24 h by those 30 normal controls during the day of maximal exercise (10.3 ± 0.9 mg/24 h) and during a day without exercise (8.5 ± 0.7 mg/24 h) were not significantly different. Albumin excretion rates were significantly higher during period II (16.9 ± 2.2 μg/min; $P < 0.001$), during period III (7.2 ± 0.8 μg/min, $P < 0.05$), and during period II and III (7.9 ± 0.8 μg/min, $P < 0.01$) than during period I (5.5 ± 0.6 μg/min). Blood pressure rose from 119.0 (±1.6)/77.7 (±1.2) mmHg to 171.2 (±2.7)/92.8 (±1.5) mmHg at the end of maximal exercise, and the heart rate increased from 76.4 (±1.4) beats/min to 164.4 (±2.5) beats/min. Maximum workload was 194.7 ± 9.5 W. Albumin excretion per 24 h exceeded the range of normal values in one patient during the day of maximal exercise (25.0 mg/24 h) compared with a day without exercise (12.1 mg/24 h); all other values remained within the normal range.

Discussion

An increase in albumin excretion during exercise has been demonstrated both in healthy controls [maximal (*10–13*) or submaximal (*14*) exercise] and in patients [diabetics, hypertensives; maximal (*12, 13*) or submaximal (*13–19*) exercise] by various authors, whereas several authors have found no increase in albumin excretion during exercise in healthy controls (submaximal exercise: *12, 13, 15–19*) or in diabetics [maximal (*11*) or submaximal (*12*) exercise]. To summarize: increased albumin excretion was demonstrated either in healthy controls or patients during maximal exercise; and during submaximal exercise most authors showed an increase of urinary albumin excretion in diabetics but not in healthy controls. No information is available regarding the influence of a short period of maximal or submaximal exercise on 24-h urinary albumin excretion (*10–19*).

In agreement with those results, we found that the albumin excretion rate increased markedly during and shortly after maximal exercise in the present study, whereas it was only slightly increased during a later urine-collection period (1 h after the end of exercise until the next morning), and 24-h albumin excretion was not significantly increased during the day that included maximal exercise. However, a possible minor increase in urinary albumin excretion during the day with exercise could have been masked by the known high day-to-day variation (*20–25*). Indeed, one patient had slightly increased albumin excretion during the day of maximal exercise. We also saw a higher albumin excretion in daytime than overnight, in accordance with the results of other investigators (*24–27*).

We conclude that urines collected to check for albuminuria need not be discarded because of a short period of exercise during the collection period, although it is preferable to avoid exercise within that period. However, high day-to-day variation may necessitate several estimations, especially if high excretion rates have been detected. Random short-time urine collections may give misleading results because of a prior period of exercise (*28*). In addition, the effect of exercise may be more marked in patients who are already slightly albuminuric. When overnight urine is used for screening, investigators must keep in mind that albumin excretion is lower during night-time.

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CLIN. CHEM. 34/12, 2518–2520 (1988)

Pyrochemiluminescence™: Real-Time, Cost-Effective Method for Determining Total Urinary Nitrogen in Clinical Nitrogen-Balance Studies

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Total urinary nitrogen (TUN) determinations for nitrogen-balance studies were traditionally performed by the Kjeldahl method, but this method is laborious, hazardous, prone to error, and no longer widely available in most clinical laboratories. During the last several decades, urinary urea nitrogen (UUN) determinations have replaced TUN as an index of urinary nitrogen excretion in many clinical laboratories, owing to its ease of determination, decreased cost, and wide availability. However, the validity of using UUN for estimating nitrogen loss has been questioned in many disease states, owing to wide variations in the proportional amount of urea found in TUN. Chemiluminescence has been proposed as an alternative to the Kjeldahl method for TUN. TUN values obtained from 24-h urine collections measured by both micro-Kjeldahl (x) and Pyrochemiluminescence™ (y) (Antek Instruments, Inc.) techniques were comparable by linear regression analysis: $n = 97$; $r = 0.996$; $r^2 = 0.992$; $y = 1.048x - 0.606$; $P < 0.001$. Automated induction of samples and calculation of results allows up to 42 samples to be run unattended. This dramatically reduces labor and overall costs for TUN determinations, while providing a more accurate and economical assessment of nitrogen excretion than UUN in a clinical setting.

Additional Keyphrases: *economics of laboratory operation · assessing trauma · chemiluminescence*

The Kjeldahl procedure is the one most widely used for measuring nitrogen in analytical chemistry (*1*). Determination of total urinary nitrogen (TUN) reflects the extent to which protein catabolism (proteolysis) is occurring after polytrauma or surgical insult or, in some disorders, the extent to which protein malnutrition is occurring.[5] In many clinical settings, nitrogen balance determinations based on TUN data are an important component of nutrition assessments. TUN determinations by the Kjeldahl method have been criticized as being costly, hazardous, and time consuming. Today, the current micro-Kjeldahl method is safer than the older technology and, although it is slow and expensive, it is still used in many clinical laboratories for TUN determinations.

Urinary urea nitrogen (UUN), because of its lower cost, assay rapidity, and availability, has been proposed as an alternative index of nitrogen excretion for calculating nitrogen balance (*2–4*). However, the validity of using UUN for estimating nitrogen loss in many disease states (i.e., renal failure and liver disease) has been questioned (*5*).

A practical instrumental method for measuring the nitrogen content of substances by chemiluminescence was first used in the petrochemical industry to determine the nitrogen content of petroleum products (*6*). Shortly thereafter, Ward et al. (*7*), using a modified chemiluminescence analyzer, were able to adapt the concepts of chemiluminescence to measure nitrogen in biological fluids. Other studies (*8, 9*), involving 24-h human urine specimens, have shown an excellent correlation between classic Kjeldahl analysis and chemiluminescence.

Here we compare the time- and cost-effectiveness of TUN analysis by chemiluminescence with a Model 703C Pyrochemiluminescent™ nitrogen system (Antek Instruments, Inc., Houston, TX 77076) with that by traditional Kjeldahl techniques. We also expand our findings for comparison studies between the Pyrochemiluminescence and micro-Kjeldahl technique previously reported (*9*).

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Presented in part at the joint meeting of the American Association for Clinical Chemistry and the Canadian Society of Clinical Chemistry, Chicago, IL, July 13–18, 1986.

Received April 4, 1988; accepted September 2, 1988.

[5] Nonstandard abbreviations: TUN, total urinary nitrogen; UUN, urinary urea nitrogen; and PCL, Pyrochemiluminescent.