Above-Normal Urinary Excretion of Albumin and Retinol-Binding Protein in Patients with Acute Myocardial Infarction

To the Editor:

Concentrations of albumin and retinol-binding protein (RBP) in urine are more sensitive indicators of renal dysfunction in hypertensive patients than the serum creatinine concentration and the Albustix\textsuperscript{TM} reaction (Ames, Tarrytown, NY) (1). Many patients with heart failure had above-normal urinary albumin and RBP concentrations (2), and these values decreased as the patients were treated with captopril (3). Patients with diabetes mellitus often have above-normal urinary albumin and RBP (4, 5), and this might dispose them to cardiovascular events (6). We have now studied the urinary excretion of albumin, RBP, and creatinine in 22 patients admitted for acute myocardial infarction (AMI) (17 men and 4 women). One of these patients had non-insulin-dependent diabetes mellitus, two had hypertension, and two had had AMI earlier. Diagnosis of AMI was based on patients' history, determination of serum creatine kinase subunit MB, serum lactate dehydrogenase isoenzyme 1, and electrocardiograms (7) according to the World Health Organization criteria (8). The study was in accordance with the ethical standards of the Helsinki Declaration of 1975 as revised in 1983.

Of the 22 patients studied, 15 were admitted within 24 h after onset of symptoms and were grouped as early admissions; the other 7 were admitted later in the clinical course and were grouped as late admissions. Twelve were given streptokinase and two were entered into a double-blind study comparing actilyse and placebo. None of the late admissions underwent thrombolyis. All patients were given acetylsalicylic acid regularly (150–300 mg/day). The patients were mobilized gradually according to a seven-step protocol during the first week of admission (7).

Creatinine concentrations in serum and urine were measured with a photometric method (daffe). All patients had a serum creatinine concentration <120 \(\mu\)mol/L. We determined the concentrations of albumin and RBP in the first voided sample of urine by immunochemical assays on the day of admission (day 0) and in the first voided urine on days 1, 2, and 5 (5, 9) afterwards. The upper limits of the reference ranges for urinary albumin and RBP concentrations were 0.45 \(\mu\)mol/L and 0.21 mg/L, respectively (5, 9).

On the day of admission, 13 of the 22 patients had an above-normal urinary albumin concentration; 8 of the 22 had an above-normal urinary RBP concentration. The urinary albumin and RBP values correlated (Spearman \(\rho = 0.65, P = 0.001\), Spearman rank correlation coefficient test). The urinary RBP concentrations were higher in the early admission group (median 1.43, range 0.18–80.30) than the late admission group (median 0.06, range 0.04–43.0) (\(P = 0.04\), Mann-Whitney U-test, two-tailed). The urinary albumin concentrations were slightly higher in the early admissions (median 0.82, range 0.07–4.31) than in the late admissions (median 0.20, range 0.02–62.10). The urinary creatinine concentrations were similar (median 8.70 vs 6.06 mmol/L).

The urinary albumin and RBP of the early admissions decreased significantly from day 0 to day 1 and from day 2 to day 5 (\(P < 0.05\), Wilcoxon–Pratt test, two-tailed). Urinary creatinine concentrations increased slightly during the first 3 days (Table 1).

Half of the patients with AMI may have had above-normal urinary albumin and RBP concentrations in the initial phase of the cardiac event. We found a lower proportion of above-normal values in patients with hypertension and a higher proportion in patients with heart failure (1, 2). The above-normal albumin and RBP concentrations are due to dysfunction of the glomeruli and the proximal tubuli, respectively (1–3).

Most of the above-normal urinary albumin and RBP excretion in our present study was a temporary phenomenon, reflecting the initial phase of the AMI. The time course for urinary albumin and RBP concentrations after the onset of symptoms did not differ between the groups of patients given streptokinase and those not (10). Thus the above-normal urinary excretion of albumin and RBP in the acute phase of the AMI may mainly reflect transitory hemodynamic and neurohormonal changes. This phase is characterized by above-normal concentrations of norepinephrine, renin, angiotensin-converting enzyme, and aldosterone; the neurohormonal activation begins to subside within the first 72 h (11).

Although mobilization of the patients during the first week of hospitalization might have increased their urinary protein excretion, other effects following the AMI seemed to more greatly decrease their concentrations of urinary albumin and RBP.

Gosling et al. suggested that the microalbuminuria of the acute phase of AMI was due to an inflammatory reaction in the renal vascular system (12). However, this explanation does not fit with the rapid reversibility of the renal dysfunctions. Above-normal urinary albumin excretion was viewed as a cardiovascular risk factor in other studies (6). But the interrelation may be more complex. Our study shows that the acute events of an AMI may cause similar, albeit transitory, renal dysfunctions.

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References

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Enzyme Confusion

To the Editor:

Recently, my colleagues and I reported two analytical systems for the determination of blood lactate with dry-chemistry and sensor technology (1, 2). In both systems we used the enzyme lactate oxidase, which catalyzes the following reaction:

\[ \text{L-lactate} + \text{O}_2 \rightarrow \text{pyruvate} + \text{H}_2\text{O}_2 \]

We used the enzyme from Pediococcus sp., which is now commercially available from Asahi Chemical Industry Co. Ltd. (Shizuoka, Japan); originally, the enzyme was purified by Eichel and Rem (3). A related lactate oxidase has now become available from ICN Biochemicals Inc. (Costa Mesa, CA). The two enzymes are easily confused with each other, and with lactate dehydrogenase:

Lactate oxidase [EC 1.13.12.4; lactate 2-monooxygenase; L-lactate:oxygen oxidoreductase (decarboxylating)]

\[ \text{L-lactate} + \text{O}_2 \rightarrow \text{acetaldehyde} + \text{CO}_2 + \text{H}_2\text{O} \]

Lactate dehydrogenase (EC 1.1.1.27; L-lactate:NAD+ oxidoreductase):

\[ \text{L-lactate} + \text{NAD}^+ \rightarrow \text{pyruvate} + \text{NADH} + \text{H}^+ \]

The former, EC 1.13.12.4, is a flavoprotein and the acceptor is oxygen; the latter, EC 1.1.1.27, does not use oxygen as acceptor. Our lactate oxidase, EC 1.1.3.x, is also a flavoprotein and the acceptor is oxygen, but note that the products are pyruvate and hydrogen peroxide. We estimated lactate by use of peroxidase (which utilizes H$_2$O$_2$) to produce a quinone dye.

Wandrup and his colleagues (4) described an analytical system for lactate in which the enzyme in the reagent catalyzed the reaction:

\[ \text{L-lactate} + \text{O}_2 \rightarrow \text{H}_2\text{O}_2 + \text{pyruvate} \]

The enzyme was reported to be a flavoprotein. It is very possible that the enzyme they used was comparable to the one we used and reported in our articles. Unfortunately, Wandrup et al. identified their enzyme as EC 1.1.1.27. The enzyme we used is EC 1.1.3.x; “x” should be determined by a responsible international committee.

References


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Lipemia Interference in Beckman Diatrac Hemoglobin A$_1c$ Procedure Removed

To the Editor:

Hemoglobin A$_1c$ (HbA$_1c$) is measured in our laboratory with the Beckman (Brea, CA) Diatrac electrophoretic procedure. The method, which is simple and easy to use, produces very good resolution of the HbA$_1b$ band, which is easily quantified by densitometry. The HbA$_1b$ band is well separated from HbA$_1b$ and HbA$_1c$. Hemoglobins C, F, and S are also well separated from HbA$_1c$ and hemoglobin HbA$_0$. The 30-day-between-run precision (CV) for the method is an acceptable 5%.

HbA$_1c$ measurements do not require fasting samples. However, we found that potassium EDTA-anticoagulated whole-blood samples with gross lipemia (opaque, milky plasma, triglycerides >20 g/L) produce an artifact that is poorly separated from the HbA$_1c$ peak and thus interferes with the HbA$_1c$ measurement. The artifact, which can be seen by holding the gel over the viewing lamp of the Beckman Appraise densitometer, appears as a faint, milky band at the application point on the gel.

In investigating how to obviate this interference, we used the electrophoresis gels, reagents, and procedures supplied in the Beckman Diatrac HbA$_1c$ kit; the manufacturer’s procedure was followed without modification. Briefly, the samples were prepared by lysing in an acidified reagent; then, 0.5 µL of hemolysate was applied to the gel and electrophoresed for 35 min. The gels were scanned wet on the Beckman Appraise

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