

URINARY ALANINE AMINOPEPTIDASE ACTIVITY IN VARIOUS URINARY TRACT DISEASES

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The value of assaying urinary alanine aminopeptidase activity was examined. The activity of normal urine was below 2 IU/l. High urinary alanine aminopeptidase was found to suggest the presence of nephritis, pyelonephritis, or other nephrotoxic processes.

Key words: Urine, AAP, Kidney, Nephritis, Pyelonephritis

Alanine aminopeptidase (AAP: EC 3. 4. 11. 2) is an enzyme specific for the brush border membrane of the kidney¹⁾. Several investigators have used urinary AAP activity as an index of nephrotoxic effects caused by aminoglycosides²⁻⁴⁾. We examined whether the measurement of this enzyme could be used to assay for nephrotoxic substances. Many other pathologic conditions cause tubular damage and subsequent elevation of urinary AAP. Herein, we report the results of our screening of urinary AAP activity.

MATERIALS AND METHODS

Urine samples from outpatients, inpatients, and normal volunteers were used. The samples were centrifuged and stored at 5°C. Assay was performed as soon as possible. The incubation medium contained 2×10^{-4} moles of L-alanine-p-nitroanilide in 2 ml of 1/15 M phosphate buffer at pH 7.6 and 0.5 ml urine. After a minute of preincubation, measurement was carried out in a photometer at 20°C. The split p-nitroaniline was measured at 405 nm.

RESULTS

Fig. 1 shows the results. "Chance hematuria" means microscopic hematuria incidentally found in asymptomatic persons with normal laboratory and X-ray data. Patients with nephritis had significantly elevated AAP activity. The group with the next highest enzyme level consisted of patients with pyelonephritis, although the difference

in values of the group and of normal control group was not significant in this study.

Further analyses were performed in the presumably normal AAP groups excluding patients with nephritis and pyelonephritis. As was shown in Table 1, AAP activity in males was nonsignificantly ($p > 0.05$) higher than that in females. A significant difference in AAP values was noted between patients with proteinuria and those without proteinuria ($p < 0.01$). No significant difference in the enzyme level was detected between the urine with and without RBC or WBC.

DISCUSSION

AAP has a molecular weight of over 200,000, and is too large to pass through the glomerular membrane. Urinary AAP is therefore considered to be delivered from the brush border membrane of the proximal tubule of the kidney^{1,4,5)}. In case of a glomerular lesion, enzyme of serum origin may also be present.

In Fig. 1, all normal persons had values within 2 IU/l. Patients with hematuria along with high AAP activity may have mild nephritis. Patients with cystitis, urolithiasis, benign prostatic hypertrophy, or neoplasia associated with AAP over 2 IU/l might have pyelonephritis or some tubular damage.

Only patients with proteinuria which suggests the presence of a renal lesion had AAP values significantly different from those

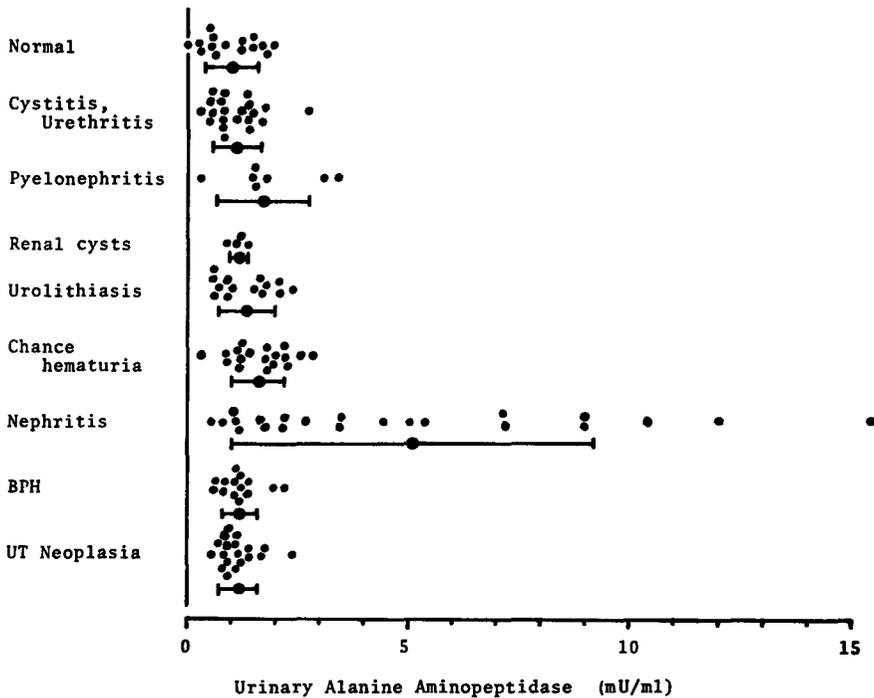


Fig. 1. Urinary alanine aminopeptidase activity in various diseases

Table 1. Urinary alanine aminopeptidase activity

Urinary AAP		Activity
		n mU/ml
Sex: Male	65	1.285±0.582
Female	40	1.132±0.553
Proteinuria: (-)	78	1.200±0.575
(+)	21	1.772±0.727*
RBC: 0	71	1.222±0.575
1- 4	14	1.561±0.827
5-19	6	1.678±0.761
over 20	8	1.600±0.700
WBC: 0- 4	81	1.254±0.548
5- 9	6	1.027±0.721
over 10	12	1.578±0.762

* $p < 0.01$

of the control group (Table 1).

Nakamura and associates⁶⁾ reported significantly elevated urinary AAP excretion in the male rat, with values of 12.7 ± 0.7 IU/g of creatinine in contrast to the 2.8 ± 0.3 IU/g of creatinine in the female rat. Urinary N-acetyl-beta-D-glucosaminidase levels examined at the same time did not show any difference with sex. Such differences with sex may also exist in man.

In this study the AAP level in pyelone-

phritis was elevated but not significantly. Burchardt⁷⁾ reported highly significant elevation after the administration of X-ray contrast medium or mannitol to patients with pyelonephritis. The same loading in normal persons did not influence urinary AAP activity. Intravenous urography combined with urinary AAP assay may therefore be of clinical interest.

Although AAP activity per ml of urine was used in this study, the concentration of AAP varied with urinary volume. Daily enzyme excretion or enzyme activity per g of creatinine is a more reliable indicator. We are using these values as indicators of nephrotoxicity. In this paper the potential role of urinary AAP activity in screening for urinary tract diseases using a single urine sample was studied. Urinary AAP activity is a subtle index of tubular or glomerular damage. Many nephrotoxic substances cause transient elevation in the values of this enzyme. If high urinary AAP is detected nephritis, pyelonephritis, or other nephrotoxic processes may be present.

REFERENCES

- 1) Scheberich JE, Falkenberg FW, Mondorf AW, Muller H and Pfeleiderer G: Biochemical and immunological studies on isolated brush border membranes of human kidney proteins. *Clin Chim Acta* 55: 179~197, 1974
- 2) Mondorf AW, Breier J, Hendus J, Scherberich JE, Mackenrodt G, Shah PM, Stille W and Schoeppe W: Effect of aminoglycosides on proximal tubular membranes of human kidney. *Europ J Clin Pharmacol* 13: 133~142, 1978
- 3) Mondorf AW: Investigations on the potential nephrotoxicity of cefazedone and gentamicin and of their combination, in comparison with the combination of cefazolin and cephalothin with gentamicin. *Arzneimittel-Forschung* 29: 449~452, 1979
- 4) Davey PG and Geddes AM: Study of alanine aminopeptidase excretion as a test of gentamicin nephrotoxicity. *J Antimicrob Chemoth* 11: 455~465, 1983
- 5) Peters JE, Rehfeld N, Schneider I, Battke H and Haschen RJ: Abgrenzung von Nieren- und Serumfraktion der Alanineaminopeptidase. *Clin Chim Acta* 24: 314~315, 1969
- 6) Nakamura M, Miyata K, Tamura T and Kawabata T: Sex difference in urinary excretion of alanine aminopeptidase in the rat. *Jap J Nephrol* 23: 209~212, 1981
- 7) Buchardt U: Alaninaminopeptidaseausscheidung in Harn nach Gabe lysosomotroper Substanzen by Patienten mit latenter und florider Pyelonephritis. *Zshr Urol* 70: 7~11, 1977
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和文抄録

種々尿路疾患における尿中 Alanine Aminopeptidase 活性

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尿中 Alanine aminopeptidase 活性を尿路疾患のスクリーニングに利用できないかと考えて検討した。正常では2単位/l以下であり、活性値の上昇は腎炎、

腎盂腎炎、あるいはなんらかの腎障害を示唆する。チャンス蛋白尿で本酵素活性が高値なときは腎炎などの可能性を示唆する。