Renal markers for assessment of renal tubular and glomerular dysfunction

Dejan Spasovski*

Department of Rheumatology, University Clinical Centre, Skopje, Republic of Macedonia

ARTICLE INFO

Article Type:
News and Views

Article History:
Received: 25 April 2013
Accepted: 21 June 2013
ePublished: 1 July 2013

Keywords:
Proximal tubule
Enzyme
Kidney

There are approximately 40 different enzymes in the urine with different origin. They originate from the kidneys, urinary tract epithelium and urinary tract glands, plasma and blood cells (1). Subcellular locations of these enzymes are:

1. Membranous (Alanine Amino Peptidase; AAP, \( \gamma \)-glutamyl transferase; \( \gamma \)-GT)
2. Lysosomal (N-acetyl-\( \beta \)-(D)-glucosaminidase activity; NAG)
3. Mitochondrial (Malate dehydrogenase: MDH)
4. Cytoplasmic (LDH)

However, proximal tubules of the kidneys have a dominant role in their excretion. Examination of the brush border epithelium (BBE) of the proximal tubules confirms that alanine amino peptidase (AAP) (90%), alkaline phosphatase, ALP (70%) and \( \gamma \)-glutamyl transferase, \( \gamma \)-GT (50%), constitute the largest part of the total activity of these enzymes in the kidney (1). Because BBE is very sensitive to insults, these and other enzymes can be used as markers for secondary renal damage in the setting of different diseases, medicines and toxins (2). Increased enzymatic activity can be a reflection of disease activity and of the residual functional capacity of the kidney.

Elevation of the urinary enzymes may indicate renal tubular damage. Urinary enzymes such as microsomal AAP and \( \gamma \)-GT can be used to detect early acute renal tubular damage which may be provoked by immunosuppressive medications, contrast media, antibiotics and chronic inflammatory disorders such as rheumatoid arthritis. Renal tubular damage could be a visceral manifestation of systemic diseases too (3).

The standard routine parameters which are used for assessment of glomerular filtration rate (GFR); have a relatively low sensitivity due to the large functional renal reserve (4). Up to 50% of renal functional capacity would be lost before any increase in blood urea nitrogen and appearance of proteinuria. Renal function and integrity can be determined by many methods such as immune, radiologic, cytological analyses, but an important modality is biochemical analyses, as non-invasive methods which have a major role in the early detection of some pathological conditions. The regulation of activity of enzymes and their isoenzymes in urine is very important because their activity in serum has small diagnostic value.

Implication for health policy/practice/research/medical education

There are approximately 40 different enzymes in the urine with different origin. They originate from the kidneys, urinary tract epithelium and urinary tract glands, plasma and blood cells. Increased enzymatic activity can be a reflection of disease activity and of the residual functional capacity of the kidney.

Please cite this paper as: Spasovski D. Renal markers for assessment of renal tubular and glomerular dysfunction. J Nephropharmacol 2013; 2(2): 23-25.
Alanine aminopeptidase (AAP) similar like leucine peptidase, hydrolyzes to peptides, amids and p-nitroanilide. During hydrolyzation of peptides N-terminal amino acid is separated. The catalytic concentration of AAP is directly proportional to the absorption of p-nitroanilide measured on 405 nm. (Reference rates: AAP in urine 0.25-0.75 U/mmol creatinine).

AAP is found in many tissues, such as kidneys, intestine, lung and liver. AAP in different organs has different electrophoretic conductivity. This enzyme has at least five different isoenzymes that could be separated from each other electrophoretically, with ion change chromatography or immunologically. In normal serum only one isoenzyme is found, while in hepatobiliary or pancreatic disease additional fractions are found. The enzyme is detected in urine.

Ethical considerations
Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

Funding/Support
None.

References
1. Vanderlinde RE. Urinary enzyme measurements in the diagnosis of renal disorders. Ann Clin Lab Sci 1981; 11: 189–201.
2. Viereger PP, Swaak AJ. Urine- and serum beta 2-microglobulin in patients with rheumatoid arthritis: a study of 101 patients without signs of kidney disease. Clin Rheumatol 1989; 8: 368-74.
3. Bailie GR, Uhlig K, Levey AS. Clinical practice guidelines in nephrology: evaluation, classification, and stratification of chronic kidney disease. Pharmacotherapy 2005; 25: 491-502.
4. Chiu JSP. Models used to assess renal function. Drug Level Res 1994; 32: 247-55.
5. Mueller PW. Detecting the renal effects of cadmium toxicity. Clin Chem 1993; 39: 743-5.
6. Maruhn D, Paar D, Bock KD. Lyosomal and brush border membrane enzymes in urine of patients with renal artery stenosis and with essential hypertension. Clin Biochem 1979; 12: 228-30.
7. de Geus HR, Fortrie G, Betjes MG, van Schaik RH, Groeneveld AB. Time of injury affects urinary biomarker predictive values for acute kidney injury in critically ill, non-septic patients. BMC Nephrol 2013; 14: 273.
8. Price RG. Urinary enzymes, nephrotoxicity and renal disease. Toxicology 1982; 23: 99-134.
9. Johnston ID, Jones NF, Scoble JE, Yuen CT, Price RG. The diagnostic value of urinary enzyme measurements in hypertension. Clin Chim Acta 1983; 133: 317-25.
10. Sandberg T, Bergmark J, Hultberg B, Jagenburg R, Trollfors B. Diagnostic potential of urinary enzymes and beta 2-microglobulin in acute urinary tract infection. Acta Med Scand 1986; 219: 489-95.
11. Kuni CM, Chesney RW, Craig WA, Albert A, England MD, De Angelis C. Enzymuria as a marker of renal injury and disease. Studies of N-acetyl-b-D-glucosaminidase in the general population and in patients with renal disease. Pediatrics 1978; 62: 751-60.
12. Neufeld EF. Natural history and inherited disorders of a lysosomal enzyme, beta-hexosaminidase. J Biol Chem 1989; 264: 10927-30.
13. Robinson D, Stirling JL. N-Acetyl-beta-glucosaminidases in human spleen. Biochem J 1968; 107: 321-7.
14. Price RG, Dance N. The demonstration of multiple heat stable forms of N-acetyl-b-glucosaminidase in normal human serum. Biochem Biophys Acta 1972; 271: 145–53.
15. Lockwood TD, Bosmann HB. The use of urinary N-acetyl-beta-glucosaminidase in human renal toxicology I. Partial biochemical characterization and excretion in humans and release from the isolated perfused rat kidney. Toxicol Appl Pharmacol 1979; 49: 323-36.
16. Gibey R, Dupond JL, Henry JC. Urinary N-acetyl-beta-D-glucosaminidase (NAG) isoenzymes profiles: a tool
for evaluating nephrotoxicity of aminoglycosides and cephalosporins. Clin Chim Acta 1984; 137: 1-11.
17. Paigen K, Peterson J. Co-ordination of lysosomal enzyme excretion in human urine. J Clin Invest 1978; 61: 751-62.
18. Bourbouze R, Bernard M, Baumann FC, Pérez-González N, Martin-Barrientos J, Cabezas JA. Subcellular distribution of N-acetyl-beta-D-glucosaminidase isoenzymes in the rabbit kidney cortex. Cell Mol Biol 1984; 30: 67-74.
19. Price RG. Measurement of N-acetyl-b-glucosaminidase and its isoenzymes in urine, methods and clinical applications. Eur J Clin Chem Clin Biochem 1992; 30: 693-705.
20. Price RG. The role of NAG (N-acetyl-beta-D-glucosaminidase) in the diagnosis of kidney disease including the monitoring of nephrotoxicity. Clin Nephrol 1992; 38: 14-9.
21. Tucker SM, Pierce RJ, Price RG. Characterization of human N-acetyl-beta-D-glucosaminidase isoenzymes as an indicator of tissue damage in disease. Clin Chem Acta 1980; 102: 29-40.
22. Mogensen CE, Chachati A, Christensen CK, Close CF, Deckert T, Hommel E, et al. Microalbuminuria: an early marker of renal involvement in diabetes. Uremia Invest 1986; 9: 85-95.
23. Rowe DJ, Dawnay A, Watts GF. Microalbuminuria in diabetes mellitus: review and recommendations for the measurement of albumin in urine. Ann Clin Biochem 1990; 27: 297-312.