Kidney Aminopeptidases A and N in Uranyl-Nitrate-Induced Acute Renal Failure

Table 1. Enzyme activity of APA and APN in uranyl-nitrate-induced ARF

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Dear Sir,

It is generally accepted that injury of renal tubular cells is the main characteristic of ischemic and toxic acute renal failure (ARF) [1]. The consequences of this injury are often dysfunction and necrosis of the tubular epithelium. Although the mechanisms responsible for development of ARF are relatively well understood, there are not enough data about molecular events related to this entity. Development of nephrotoxic ARF is characterized by alteration in sodium absorption and glomerular hemodynamics, activation of the renin-angiotensin system and decreasing glomerular filtration rate [1]. Biochemical abnormalities such as rapid depletion in cellular adenosine triphosphate, increase in cytosolic calcium, generation of free radicals, acidosis and activation of phospholipases and proteases also follow the course of ARF [2]. Aminopeptidase A (APA, EC 3.4.11.7) and aminopeptidase N (APN, EC 3.4.11.2) are cell surface proteases mainly located on the brush border of the tubular epithelium and glomerular cells [3-5]. These two ectoenzymes involved in processing of different stimulatory and inhibitory oligopeptides represent a possible regulator of cellular growth and differentiation.

In this study activities of APA and APN were investigated in uranyl-nitrate-induced ARF. Experimental ARF was induced by a single dose of uranyl nitrate (10 mg/kg b.w.) injected intraperitoneally into male Wistar rats weighing 150-180 g [6]. Seventy-two hours after challenge of experimental ARF, the animals were sacrificed. The level of plasma creatinine was 237.00 ± 48.15 versus control 75.33 ± 5.71 µmol/l (p < 0.001) and the blood urea level was 20.80 ± 4.92 versus control 4.46 ± 0.61 mmol/l (p < 0.001). APA and APN activities were measured in 10% homogenate of cortex and medulla, and in 24-hour urine from the hydrolysis of 10mM α-glutamyl-β-nitroanilide (APA) and 1.5 mM alanine-β-nitroanilide (APN) as substrates. APA in the kidney cortex, medulla and urine was significantly decreased (p < 0.001)
compared to the control (table 1). Activity of APN was significantly decreased only in the medulla and urine (p < 0.05).

The results of this study indicate that in uranyl-nitrate-induced ARF activities of APA and APN are reduced. Consequently, processing of tubular proteins by APA and APN is damaged in ARF. This diminished activity in the renal cortex and urine could be the result of a proposed high uranyl nitrate nephrotoxicity. Cell damage, estimated by serum lactate dehydrogenase activity, is almost 2.5 times higher in a uranyl-nitrate-treated group than in controls (data not presented). A prominent characteristic of this investigation is the reduction of APA activity 72 h after induction of experimental ARF, especially in the kidney cortex. The primary cause of this decreased APA activity may be activation of the renin-angiotensin system during the early phase of acute renal injury, when the production of angiotensin II is increased, or it is due to injury of proximal tubular epithelial cells [7].

Considering angiotensin II as the main substrate of APA (angiotensinase A) in the kidney, this reduction of APA activity can have consequences for renal hemodynamics.

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