Management of Acute Nephritis with the Epsilon-Aminocaproic Acid Fact or Epiphenomenon?

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Dear Sir,

Our interest in the antinephritic potential of E-aminocaproic acid (EACA), a drug of established anti-inflammatory properties [1], goes back to the incidental observation of striking and abrupt subsidence of nephrotic syndrome in a patient treated with EACA for life-threatening hematuria after renal biopsy [2]. A similar effect was encountered in our institute on two other occasions, under comparable circumstances [unpubl. observations]. Therefore, in a pilot experimental study we assessed the ability of EACA to reduce nephrotoxic serum nephritis in LEW rats [3]. Combined oral and intraperitoneal administration of the drug (1 g/kg), starting from the day of glomerulonephritis induction, resulted in significant attenuation of renal histopathology, decrease in proteinuria and improvement of kidney function.

In order to further substantiate the above observations we recently conducted a study using an experimental model of toxic immune nephropathy induced in BN rats by subcutaneous injections of mercuric chloride (200 µg/100 g body weight every 72 h) (fig. 1). This procedure causes polyclonal B cell activation with subsequent development of anti-GBM glomerulonephritis followed by immune complex nephropathy, renal failure and animal death in over 75% of cases [4]. Severe impairment of kidney function, scarce histologic glomerular abnormalities and a protracted course differentiates this model from nephrotoxic serum nephritis evaluated

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Fig. 1. Proteinuria and endogenous creatinine clearance (Ccr) in control nephritic (II, n = 10) and nephritic EACA-treated (H, n = 10) rats with HgCl₂ nephropathy. Proteinuria assessed on days 8/9, 13/14, 17/18 and 21/22 (a): *p < 0.025, ↔p < 0.01, ***p < 0.0005. Ccr calculated from serum creatinine and 24 h creatinine excretion on day 21/22 (b). Values are means ± SD.

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previously. Moreover, in this study we commenced administration of EACA on day 9 after the first injection of HgCl₂, contrary to the induction day 0 in the previous experimental design. Furthermore, in these settings the EACA exerted a remarkably beneficial effect [administration protocol, the same as in 3], reducing animal mortality, proteinuria and enhancing creatinine clearance (both p < 0.0005, day 22) with notable decrease in intensity of interstitial mononuclear cell infiltrates. Distribution or density of glomerular autologous IgG deposits was unaffected by EACA and no thrombus formation was revealed by autopsy in experimental rats. We infer from these findings that EACA ameliorates inflammatory renal injury without significant modification of its immune induction. Although the exact mechanism of this effect cannot presently be determined, the antifibrinolytic potential of EACA could presumably not be implicated since fibrinolysis is regarded as protective against glomerulonephritis [5]. Conversely, the drug interference with inflammatory proteolytic cascade activation (complement system, kininogenesis, neutral proteinases) could potentially be of relevance. This issue is currently under evaluation in our laboratory.

References

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