Effects of N-Acetylcysteine on Angiotensin-Converting Enzyme Plasma Activity in Patients with Chronic Kidney Diseases

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In one of the previous issues of *Blood Purification* Sahin et al. [1] reported that N-acetylcysteine (NAC) could improve endothelial dysfunction in patients with chronic kidney disease (CKD). The authors suggested that this effect is related to the action of NAC as an antioxidant, i.e. free-radical scavenger, or as a reactive sulfhydryl compound that increases the reducing capacity of the cell. Here, we would like to extend these observations and present the results of our recent clinical study which indicate that NAC could also interfere with the renin-angiotensin system reducing the concentration of circulating angiotensin-converting enzyme (ACE). In a placebo-controlled, randomized, open two-period cross-over study, we evaluated the influence of NAC on plasma concentration of ACE in 20 nondiabetic patients with persistent proteinuria (0.4–6.36 g per 24 h) with normal or slightly lowered kidney function (eGFR 61–163 ml/min). Subjects entered the 8-week run-in period during which antihypertensive therapy was settled with a target blood pressure below 130/80 mm Hg. Next, patients were

randomly assigned to one of two treatment sequences: 8 weeks NAC (1,200 mg/day)/8 weeks washout/ 8 weeks placebo (sequence 1) or 8 weeks placebo/8 weeks washout/8 weeks NAC (1,200 mg/day) (sequence 2). The dosages of any drugs once established in the run-in period, were left unchanged throughout the study, as well as in the washout period. Circulating ACE concentration was determined in plasma with a commercial ELISA system (Human ACE Immunoassay Quantikine, R&D Systems, Minneapolis, Minn., USA). NAC significantly reduced ACE concentration (Δ mean $\pm$ SEM) relative to placebo (-20.13 ± 8.96 vs. -7.59 ± 7.43 ng/ml; $p = 0.036$). A similar conclusion was reached previously in experimental conditions showing that different antioxidants including NAC may decrease local endothelial ACE activity [2]. The molecular and cellular mechanisms by which oxidative stress may mediate ACE activity are not clear so far. Given that increased endothelial expression of ACE plays an important role in cardiovascular remodeling [3], one may indicate that NAC not only improves endothelial

dysfunction but also prevents against vascular and myocardial structural changes. It may have a great clinical implication given that the population with CKD is at very high risk of cardiovascular complications.

References

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