THE POTENTIAL ROLE OF N-ACETYLCYSTEINE TO ATTENUATE THE OXIDATIVE STRESS EXPOSED TO UREMIC SERUM IN THE VASCULAR SYSTEM

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Introduction and objectives: Chronic kidney disease (CKD) progression is accompanied by systemic oxidative stress, which contributes to an increase in the risk of cardiovascular diseases (CVDs). N-acetylcysteine (NAC) is among the most studied antioxidants, but its therapeutic benefits in CKD-associated CVDs remain controversial. Here, we investigated whether NAC could inhibit the oxidative stress induced by uremia in vitro and in vivo. Materials and methods: Endothelial and smooth muscle cells were challenged with human uremic or non-uremic sera, and the effects of a pre-treatment with 2 mM NAC were evaluated. Reactive oxygen species (ROS) production, protein oxidation and total glutathione/glutathione disulfide (tGSH/GSSG) ratios were measured. Five-sixths nephrectomized or sham-operated rats were orally treated (in the drinking water) with 60 mg/kg/day NAC or not treated for 53 days. Plasma cysteine/cystine reduction potential Eh(Cyss/2Cys) was determined as a novel marker of the systemic oxidative stress. Results and conclusions: NAC inhibited all the determined oxidative stress parameters, likely by increasing the tGSH/GSSG ratio, in both cell lines exposed to uremic serum. Orally administered NAC attenuated the systemic oxidative stress in uremic rats. The present results indicate that NAC, by preventing GSH depletion in vascular cells exposed to uremic serum and by attenuating the systemic oxidative stress during CKD progression, emerges as a potential strategy to prevent the oxidative stress induced by uremic toxicity in the vascular system.

Key Words: Oxidative stress, Uremia, N-acetyl cysteine.