Investigating the volume status before contrast nephropathy studies

Sir,

We read with great interest the original article by Drager et al. [1] about the mechanism of a protective effect of N-acetylcysteine (NAC) against contrast-induced nephropathy (CIN) in patients undergoing elective coronary angiography. This study assessed pre- and post-radiocontrast NAC effects on specific oxidative stress and renal tubular injury markers. CIN is one of the well-recognized risks of coronary angiography. Contrast-related risk factors include excess dose or repeated doses of contrast volume and the use of ionic and high-osmotic agents. Patient-related risk factors include pre-existing renal insufficiency, diabetes mellitus, advanced age, congestive heart failure, concomitant administration of drugs that interfere with the regulation of renal perfusion and any condition associated with decreased effective circulating volume [2]. Volume status is very important in the development of CIN [2,3]. The study by Drager et al. was not designed to detect the volume status of patients before the angiography. All the patients in both groups were hydrated with the same hydration regimen (2 ml/kg body weight/h from 4 h pre- until 4 h post-angiography). Information related to volume in this study revealed only that study participants were not permitted diuretic medications along with hydration therapy and patients diagnosed with pulmonary oedema were excluded. In the study design it was shown that one patient from the placebo group with acute pulmonary oedema during saline infusion was excluded from the study. This means that the groups were not homogeneous for volume status. The two groups were similar regarding demographics, body mass index, medication and volume of radiocontrast administered. However, the ages of the study participants ranged from 18 to 80 years and no data were provided on left ventricular ejection fraction (LVEF). Drager et al. found that comparing creatinine clearance values before and after angiography, a significant increase was seen in NAC patients, whereas placebo patients presented no change. After radiocontrast, urinary 15-isoprostane F2, levels in placebo patients increased significantly over baseline values, whereas urinary 15-isoprostane F2, levels in NAC patients remained basically unchanged. Furthermore, NAC treatment led to lower levels of \( \alpha \)-glutathione S-transferase than placebo treatment did. If a patient has fluid loss or decreased oral fluid intake, especially in old patients with low LVEF, the creatinine clearance and serum creatinine might be affected more than in normovolemic patients, patients have a higher risk for CIN than others, and parameters such as oxidative stress and proximal tubular injury markers may be changed in these patients [2–4]. For this reason, the method used in the study by Drager et al. is not sufficient to discuss the effect of NAC on the renal tubular effect and oxidative stress. Acetylcysteine, have been shown to be renoprotective in some studies but not in others. In a further recently published meta-analysis of 11 studies, no benefit of NAC in reducing the risk of CIN in patients with baseline renal dysfunction was found [3]. When we look at the study design of these NAC studies, we see that there is a lack of volume status of patients before the coronary angiography. We think the lack of volume status in these studies is one of the causes of the different results with NAC.

Clinical parameters of hydration are not always reliable. Several methods for the estimation of hydration have been reported. Significant correlation was found between inferior vena cava diameter and inferior vena cava collapse index, mean atrial pressure, total body volume as determined by the radioiodinated serum albumin method and electrical bioimpedance. The non-invasive prediction of pulmonary-capillary wedge pressure is important for the recognition and treatment of a variety of cardiovascular disorders [4,5]. The combination of clinical parameters and any of these methods might accomplish a more accurate evaluation of the hydration in patients in CIN studies.

Conflict of interest statement. None declared.

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doi:10.1093/ndt/gfh609

Reply

Sir,

Toprak and Cirit propose that assessing volume status is essential to evaluating possible strategies for preventing contrast-induced nephropathy (CIN), since any condition associated with a reduction in circulating volume may be a potential risk factor for CIN. The authors also note the lack of volume status assessment in clinical studies of CIN.