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Acetylcysteine Induces an Increase in Renal Blood Flow after Contrast Admission that is Lost in Target Patients with Chronic Kidney Disease

Background: Radiocontrast-induced nephropathy (RCIN) is an important complication of imaging, increasing mortality 3-fold in chronic kidney disease (CKD) patients receiving contrast. The pathophysiology of RCIN is poorly understood but the most commonly cited mechanism involves reduced renal blood flow (RBF) leading to acute tubular necrosis. Oral acetylcysteine (NAC) has been widely used for prevention since a publication in 2000 but evidence for benefit is limited, despite many randomised controlled trials (RCTs). Of note, there have been no detailed clinical studies investigating the effect on renal function of large intravenous (IV) and standard oral NAC doses that might guide design of RCTs. We aimed to assess the effect of oral and IV NAC on renal function, with or without contrast.

Methods: We performed a structured set of randomised cross-over and parallel-group studies to assess the effect of oral and IV NAC on normal and diseased (CKD stage III) kidneys, with and without iso-osmolar contrast (iodixanol). Eight patients were recruited to each of three cross-over studies comparing oral NAC (1200 mg BD for two days) and IV NAC (200 mg/kg over 7 hours) with placebo in 1) volunteers with normal kidneys, 2) volunteers with normal kidneys receiving 100 mL contrast, and 3) patients with CKDIII not receiving contrast. Sixty-six patients were recruited to a 4th parallel group RCT, assessing the effect in patients with CKDIII receiving contrast for elective coronary angiography. We recorded systemic and renal haemodynamics in all patients, and biomarkers of renal injury (plasma creatinine and cystatin C, urinary NGAL and KIM-1) for up to 72 hrs in CKD III patients receiving contrast for elective coronary angiography.

Results: In healthy volunteers, IV NAC, but not oral NAC, increased blood pressure (SBP: +8 ± 5 mmHg, p=0.003 vs. placebo) and heart rate ((by +4.0 ± 1.2 bpm, p<0.0001 vs. placebo) and caused renal vasodilatation with an increase in RBF (+111 ± 44 mL/min, p=0.003 vs. placebo)) and glomerular filtration rate (GFR; +2 ± 3 mL/min/1.73m^2, p<0.0001 vs. placebo). This effect on renal haemodynamics was increased and sustained in the presence of radiographic contrast (+125 mL/min, p<0.05 vs. placebo). In patients with diseased kidneys, however, IV NAC caused only a rise in heart rate, with no effect on blood pressure, RBF or GFR. Oral NAC had no effect on any variable. In CKD III patients receiving contrast during angiography, IV NAC reduced a modest fall in blood pressure that occurred in other groups just after contrast administration. There was no significant effect on RBF, GFR, or markers of renal injury.

Conclusion: High dose IV NAC caused a marked increase in RBF in healthy volunteers that was increased further in the presence of contrast. Unfortunately, this effect did not occur in CKD III patients, a group that might benefit from such an effect of IV NAC, likely due to endothelial dysfunction in CKD patients. Intravenous NAC resulted in no improvement in renal biomarkers after administration to CKD III patients undergoing coronary angiography. We found no evidence that high-dose NAC administered by the IV route, or standard dose NAC administered by the oral route, offer any renoprotective benefit to patients with CKD III. This study emphasises again the importance of detailed mechanistic clinical studies before progressing to initiating RCTs for a novel intervention.