



# Is There Sufficient Evidence to Support the Use of Intravenous N-acetylcysteine for the Prevention of Contrast Induced Nephropathy?



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## Abstract

We discuss the safety of efficacy of using intravenous N-acetylcysteine for the prevention of contrast induced nephropathy. Herein we discuss the relevant literature and provide evidenced-based recommendation.

**Keywords:** N-acetylcysteine; NAC; Contrast induced nephropathy; CIN

**Abbreviations:** NAC: N-acetylcysteine; CIN: Contrast Induced Nephropathy; CT: Computed Tomography; SCr: Serum Creatinine Clearance

## Introduction

Is there sufficient evidence to support the use of intravenous N-acetylcysteine for the prevention of contrast induced nephropathy? Basically, the answer is a simple yes and no, depending on the clinical situation, the patient and the radiological study or procedure in question. Accordingly, we reviewed some recent literature regarding N-acetylcysteine (NAC) for the prevention of contrast induced nephropathy (CIN) in an attempt to resolve in part this issue. We conclude with some basic suggestions regarding its use.

## Discussion

Radiocontrast-induced nephropathy is a serious complication regarding iodinated intravenous contrast. Commonly used contrast agents for cardiac angiography and computed tomography (CT) include iodixanol (Visipaque) and iohexol (Omnipaque). Visipaque has an osmolality similar to serum and has been reported to have lower incidence of contrast-induced nephropathy and can be used in patients with creatinine of 2.0 and lower. Omnipaque is typically used in patients with normal kidney function. Although there is no single consensus for contrast-induced nephropathy, many studies define CIN as a 25% relative or 0.5 mL/min increase in serum creatinine clearance (SCr). Risk factors are manifest and

include advanced age, existing renal disease, diabetes mellitus, CHF, and dehydration. The exact mechanism for CIN is unknown and probably has many causes including vasoconstriction leading to medullary ischemia, direct cytotoxicity of contrast, and production of reactive-oxygen species have all been posited as potential causes. Prevention of CIN has been of interest given the complications of long-standing renal impairment [1].

N-acetylcysteine has been at the forefront of agents used to decrease the risk of CIN associated with the use of IV radio contrast. The first study to address this issue found a reduction in CIN in patients receiving NAC before and after imaging studies [1]. However, this randomized-control study has been inconsistently reproduced, with larger and more recent studies showing no benefit of NAC in reducing CIN compared to placebo [2]. Oral NAC is well absorbed, tastes bad, and undergoes extensive first-pass kinetics, particularly by deacetylation to cysteine. Bioavailability of NAC is variable and ranges from 3-20%. However, decomposition products of NAC are strong antioxidants, which themselves may play a limited role renal protection. The use of IV NAC has several advantages including its use emergently, especially for unplanned cardiac catheterizations and in obtunded patients needing imaging

studies or treatment for acetaminophen overdoses. A 6-gram vial of IV NAC costs significantly more (as much as 8-10 times more) compared to an equivalent quantity of the oral formulation costs.

There is a decreased financial burden with oral administration, which is why it has been advocated by many. Many of the studies regarding the use of IV NAC in prevention of CIN report variable results. In patients at risk for CIN (baseline serum creatinine  $\geq 1.36$ ), studies have showed NAC to be superior to IV hydration alone in patients undergoing cardiac catheterization [3]. However, other randomized control trials have shown no difference in serum creatinine (SCr) in the NAC or placebo arms in patients undergoing angiography [4]. Only one study was conducted to measure the effects of IV NAC on SCr and the biomarker cystatin C for patients undergoing CT scans. This study reported a 21% incidence of CIN in the IV hydration arm but only 5% CIN in the NAC arm based solely on SCr; however, based on cystatin C, both groups showed equivalent increases in renal impairment [5]. Based on this study, it can be agreed that serum creatinine is not the best marker for assessing acute contrast induced nephropathy and that other more sensitive (and more temporal) markers should be considered.

## Conclusion and Summary of recommendations

Based on the current literature and state of the art, the following recommendations are proposed.

- i. IV NAC is not to be used in patients undergoing CT scans or cardiac angiography without known risk factors for contrast-induced nephropathy.

- ii. IV NAC can be considered for patients undergoing coronary angiography with multiple risk factors for contrast-induced nephropathy (Creatinine clearance  $< 60$  mL/min) and receiving high volumes of contrast (greater than 200 mL).

- iii. High dose IV NAC can be used (1200 mg x 5 doses) when IV NAC is indicated as described above.

Proper hydration should be ensured in all patients regardless of the need for NAC.

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