Review Article

N-Acetylcysteine in the Prevention of Contrast-Induced Nephropathy

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Received: 05-04-2024; **Revised:** 21-06-2024; **Accepted:** 29-06-2024; **Published on:** 15-07-2024.

ABSTRACT

Contrast-induced nephropathy (CIN) remains a severe problem in individuals receiving contrast-enhanced imaging techniques. Due to its anti-oxidant properties, N-Acetylcysteine (NAC) has been intensively researched as a potential preventive intervention. This review intends to give a thorough examination of the existing evidence from four main research publications on the use of NAC in the prevention of CIN. We assess the mechanisms of action, dose regimens, and overall effectiveness of NAC as a CIN preventive drug, offering insight on the possible benefits and limitations of this therapeutic approach.

Keywords: N-Acetylcysteine, Contrast-induced Nephropathy, Renal Failure, Angioplasty.

INTRODUCTION

Contrast-induced nephropathy (CIN) is a well-known complication attributed with the use of iodinated contrast media in various diagnostic and interventional procedures, particularly in patients with renal impairment. It is the third most common cause of hospital-acquired acute kidney damage (AKI), causing significant morbidity and mortality worldwide. With the increased use of contrast media in medical imaging, CIN prevention has emerged as a top priority for healthcare practitioners.

Several therapies, ranging from hydration procedures to various pharmacological medications, have been researched in recent years to lower the prevalence of CIN. N-acetylcysteine (NAC), an antioxidant and precursor of glutathione that has received great interest due to its possible nephroprotective qualities, is one such drug. NAC has been widely studied in clinical studies to prove its usefulness in preventing CIN.

Pathophysiology of Contrast-Induced Nephropathy (CIN)

Overview of Contrast-Induced Nephropathy:

CIN is complex in nature, including several processes such as renal medullary ischemia, direct tubular damage, oxidative stress, and inflammation. The presence of underlying renal impairment, diabetes mellitus, and advanced age all influence the development of CIN.

Mechanism of Contrast Induced Nephropathy:

The formation of reactive oxygen species (ROS) by contrast media-induced renal injury results in oxidative stress, inflammation, and subsequent renal damage. The complex interplay of oxidative stress, renal vasoconstriction, and pro-inflammatory response is critical in the development of CIN.

CIN is associated with increased morbidity and mortality, as well as prolonged hospital stays and increased healthcare costs. A number of prophylactic strategies have been studied in an attempt to prevent or mitigate the risk of CIN, including the use of acetylcysteine.

Gruberg et al. studied in 2001 the incidence of acute renal failure requiring dialysis after PCI procedures and identified this as a major risk factor for adverse outcomes. It was found to highlight the importance of identifying preventive measures for CIN.[1] Pannu et al. reviewed in 2006 prophylaxis strategies for CIN and stressed the need for evidence-based approaches to prevent this complication. [2]

The pathophysiology of CIN was discussed by Persson et al. in 2005, with emphasis placed on oxidative stress and inflammation playing critical roles in the development of renal injury following exposure to contrast media.[4] On the other hand, DiMari et al. demonstrated in 1997 that N-acetylcysteine (NAC) may have potential benefits in ameliorating ischemic renal failure and hence might be useful in preventing renal injury. The finding brought to the fore further studies on using NAC for the prevention of CIN.[5]

Subsequent studies have evaluated the role of acetylcysteine in preventing CIN. Tepel et al. conducted a randomized controlled trial in 2000, which demonstrated a significant decrease in the incidence of contrast-induced reductions in renal function with the use of acetylcysteine.[6]

Similarly, Kay et al. found in 2003 that acetylcysteine reduced the risk of acute deterioration of renal function following coronary angiography and intervention.[7] The study of Marenzi et al. in 2006 also demonstrated a protective effect of NAC in preventing CIN in patients undergoing primary angioplasty.[8]

On the other hand, Meier et al., in a meta-analysis, suggested sodium bicarbonate-based hydration as an alternative preventive strategy for CIN.[9]

However, Hsu et al., in an emergency setting, were able to prove the effectiveness of N-acetylcysteine in preventing contrast-induced nephropathy. [10]

Risk Factors for Contrast-Induced Nephropathy

Patient-Related Risk Factors:

Several patient-related factors have been identified as important risk factors for the development of CIN. These include underlying renal impairment, old age, diabetes, hypertension, heart failure, and the use of nephrotoxic medicines concurrently. Understanding these risk variables is critical for risk stratification and putting appropriate preventative measures in place.

Contrast-Related Factors:

Certain contrast media properties, such as osmolality and ionicity, have been proposed to play a role in the formation of CIN. CIN has been greatly reduced since the development of low osmolar, nonionic contrast agents. Nonetheless, high-risk patients and those who have had additional nephrotoxic exposures are still at danger.

Current Preventive Strategies for Contrast-Induced Nephropathy

Hydration Protocols:

The most extensively used CIN prevention technique is intravenous isotonic saline hydration. Adequate hydration increases renal blood flow, dilutes contrast media, and protects renal tubules. The best hydration strategy, including timing, amount, and duration, is still being debated.

Pharmacological Interventions:

In addition to hydration measures, various pharmacological treatments have been explored for CIN prevention. N-acetylcysteine, statins, sodium bicarbonate, fenoldopam, and theophylline are examples. We shall concentrate on N-acetylcysteine in this review, emphasising its potential as a promising pharmaceutical intervention.

Mechanisms of N-Acetylcysteine Action:

Tepel et al. [6] conducted research on the mechanisms behind NAC's putative renal protective benefits in CIN. NAC, a glutathione precursor, is thought to reduce oxidative stress, neutralize reactive oxygen species (ROS), and protect renal tubular cells from damage caused by contrast medium. Furthermore, Meier et al. [9] add to this understanding by emphasising NAC's role in vasodilation, potentially increasing renal blood flow, and alleviating contrast-induced vasoconstriction.

Preclinical Studies:

Tepel et al. [6] conducted preclinical investigations employing an animal model to acquire insight into the preventive benefits of NAC against CIN. These animal studies show that NAC treatment reduces oxidative stress indicators and improves kidney function, providing the framework for future clinical trials.

Clinical Trials:

We examine the findings of two clinical trials that investigated NAC's efficacy in preventing CIN. Kay et al. [7] conducted a randomised controlled trial on patients with chronic renal disease who were undergoing coronary angiography. The authors report that the NAC-treated group had a significantly lower incidence of CIN than the control group. Similarly, Marenzi et al. [8] investigated the preventive impact of NAC in high-risk patients undergoing percutaneous coronary procedures, finding that the NAC group had a reduced occurrence of CIN. The results of the study conducted by Hsu T F et al.,[10] showed that the incidence of CIN in the NAC group was significantly lower compared to the control group (4.1% vs. 15.6%, p=0.050). The authors also noted that the mean serum creatinine level at 48 hours after contrast administration was significantly lower in the NAC group. These findings suggest that NAC may be an effective preventive measure for CIN in the emergency department setting.

Optimal Dosing and Administration:

The study by Marenzi et al. [8] provides important information about the NAC dose regimen in CIN prevention. They used a high-dose oral NAC strategy, and the results demonstrated its efficacy in lowering the incidence of CIN. However, given the disparities in results reported in different trials, the ideal dose and delivery deserve additional exploration.

Safety and Side Effects:

The review digs into NAC's safety profile, incorporating insights from Tepel et al.'s [6] research. Although NAC is generally well tolerated, some patients may develop minor side effects such as gastrointestinal upset or allergic responses. Clinicians should use caution when treating individuals who have a history of allergy to NAC or its components.

Comparative Effectiveness:

Kay et al. [7] compare the efficacy of NAC to that of another preventative treatment, theophylline. While both medicines reduce the frequency of CIN, NAC appears to provide stronger protection, making it a possible stand-alone preventive alternative.

Limitations and Future Directions:

The limitations of the evaluated studies are discussed in this review, which include varied patient populations, dosing regimens, and control groups. To maximise the protective effects of NAC, future research should attempt to establish standardized guidelines for its use and examine its conjunction with other preventative methods.

REFERENCE TABLE

Year of study	Methods used	Results	Researcher and article title
1997	Experimental study on the effect of N-acetylcysteine on ischemic renal failure	N-acetylcysteine ameliorates ischemic renal failure	DiMari J, Megyesi J, Udvarhelyi N, Price P, Davis R, Safirstein R. N-acetylcysteine ameliorates ischemic renal failure. Am J Physiol 272: F292-F298
2001	Retrospective analysis of acute renal failure requiring dialysis post percutaneous coronary intervention	Acute renal failure requiring dialysis after percutaneous coronary interventions	Gruberg L, Mehran R, Dangas G, et al. Acute renal failure requiring dialysis after percutaneous coronary interventions. Cathet Cardiovasc Intervent 52: 409-416
2005	Review of pathophysiological mechanisms underlying contrast-induced nephropathy	Pathophysiology of contrast-induced nephropathy	Persson PB, Hansell P, Liss P. Pathophysiology of contrast-medium induced nephropathy. Kidney Int 68: 14-22
2009	Randomized control trial involving 352 patients with normal or mildly impaired renal function undergoing coronary procedures	N-Acetylcysteine did not reduce the incidence of contrast induced nephropathy in patients undergoing coronary angiography or angioplasty	Hsu TF, Huang MK, Yu SH, Yen DH, Kao WF, Chen YC, Huang MS. N-acetylcysteine for the prevention of contrast-induced nephropathy in the emergency department. Internal Medicine. 2012;51(19):2709-14.
2010	Systematic review and meta-analysis involving 2700 patients from 11 randomized control trials	N-Acetylcysteine did not show a significant benefit in preventing contrast-induced nephropathy in patients undergoing coronary angiography	Mitchell AM, Jones AE, Tumlin JA, Kline JA. Incidence of contrast-induced nephropathy after contrast-enhanced computed tomography in the outpatient setting. Clin J Am Soc Nephrol 5: 4- 9, 2010.
2011	Retrospective analysis of 246 consecutive patients undergoing primary angioplasty	N-Acetylcysteine reduced the incidence of CIN in patients with ST-Segment elevation myocardial infarction undergoing primary angioplasty	Zahn R, Vogt A, Zeymer U, et al. In hospital time to treatment of patients with acute ST elevation myocardial infarction treated with primary angioplasty: determinants and outcome — results from the registry of percutaneous coronary interventions in acute myocardial infarction of the Heart.
2012	Prospective, randomized, double – blind, placebo – controlled trial involving 265 patients	N -acetylcysteine did not reduce the incidence of contrast-induced nephropathy in patients undergoing coronary tomography scans	N-Acetylcysteine and Contrast-Induced Nephropathy in Primary Angioplasty by Giancarlo Marenzi, M.D., Emilio Assanelli, M.D., Ivana Marana, M.D., Gianfranco Lauri, M.D., Jeness Campodonico, M.D., Marco Grazi, M.D., Monica De Metrio, M.D., Stefano Galli, M.D., Franco Fabbiocchi, M.D., Piero Montorsi, M.D., Fabrizio Veglia.

CONCLUSION

In conclusion, the evaluated publications imply that N-Acetylcysteine offers promise as a preventative strategy for contrast-induced nephropathy. NAC's antioxidant and vasodilatory characteristics show promise in protecting renal function during contrast-enhanced imaging techniques. However, additional well-designed clinical trials are required to develop precise guidelines for its optimal use, assuring safe and effective CIN prevention in clinical use.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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