Is Oral N-acetylcysteine Effective on the Prevention of Radiocontrast induced Nephropathy in Patients with Acute Renal Failure?

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Purpose: N-acetylcysteine (NAC) has been known to have protective effects on the prevention of radiocontrast induced nephropathy (RCIN) in chronic renal failure (CRF). We investigated the effects of NAC in acute renal failure (ARF).

Methods: From January to June 2006, we retrospectively enrolled patients with ARF who were checked with contrast computed tomography (CT) at an emergency department. We divided patients into the NAC group and the control group. We compared baseline demographic characteristics, underlying diseases, infused fluid volume, blood urea nitrogen (BUN), and serum creatinine (Cr) level before and after CT scan. ARF was defined as serum Cr > 1.5 mg/dL. RCIN was defined as an increase in serum Cr level of at least 0.5 mg/dL or 25% 48 hours after CT.

Results: Of a total 106 cases, 23 patients were the NAC group and 83 were the control group. There were no significant differences in baseline findings including underlying disease, cause of ARF and serum Cr level. The volume of infused fluid before and after CT were not different between the two groups (before; \( p=0.183 \) after; \( p=0.149 \)). After CT scan, BUN and serum Cr level were decreased without statistical significance in both groups (NAC vs control group: BUN; 21.0 ± 12.9 vs 20.5 ± 14.2 \( p=0.863 \) Cr; 1.3 ± 0.5 vs 1.4 ± 0.5 \( p=0.451 \)). RCIN developed in total 3 cases, 2 cases in the NAC group and 1 in the control group (\( p=0.524 \)) and one of the NAC group performed hemodialysis.

Conclusion: In case of patients with ARF, there was no protective effect of NAC on RCIN.

Key Words: N-acetylcysteine, Radiocontrast induced nephropathy, Acute Renal Failure

Introduction

Radiocontrast induced nephropathy (RCIN) is a complication of computed tomography (CT) scan and angiography in which intravenous or intraarterial contrast agent is administered. RCIN was reported to be the third most common cause of acute renal failure (ARF) in hospitalized patients\(^1\)\(^-\)\(^5\). RCIN is usually defined by a 0.5 mg/dL or 25% increase in serum creatinine (Scr) level after exposure to the contrast medium\(^6\). Risk factors for RCIN include pre-existing renal dysfunction, age over 75 years, volume depletion, diabetes mellitus, hypertension, heart failure, cirrhosis, nephrosis, volume and type of contrast agent, and concomitant administration of potentially nephrotoxic drugs such as angiotensin converting enzyme inhibitors and nonsteroidal anti-inflammatory drugs\(^7\)\(^-\)\(^10\). RCIN occurred in 11% to 45% of high risk patients and the need for dialysis ranged from 0% to 2.6%\(^11\)\(^-\)\(^15\).

The pathophysiology of RCIN remains incompletely understood. Current evidence suggests that radiocontrast agent induces prolonged vasoconstriction and medullary ischemia coupled with generation of free radicals and oxidative injury to the renal tubular cells\(^16\)\(^-\)\(^18\).

Several agents have been proposed to prevent RCIN. However, saline hydration and the use of low-osmolar or iso-osmolar radiodcontrast media have proved to be effective\(^19\)\(^,\)\(^20\). Another agent such as diuretics, mannitol, theophylline, fenoldopam and calcium channel blockade have been reported ineffective or inconclusive\(^21\)\(^-\)\(^23\).

In recent years, N-acetylcysteine (NAC) has been extensively studied to prevent RCIN. NAC was initially introduced as a mucolyticit agent and later its antioxidant property led it to use in the treatment of...
acetaminophen intoxication. In 2000, Tepel et al. reported that the use of oral NAC before and after contrast enhanced computed tomography markedly reduced the incidence of nephropathy. Since then, many studies have been conducted, but the protective effect of NAC on RCIN was controversial.

Most studies of the preventive effect of NAC on RCIN have been conducted in patients with chronic renal failure (CRF) on selective coronary angiography with strict control of the kind and volume of hydration fluid. On these background studies, we hypothesized that oral NAC would be effective on the prevention of RCIN in patients with ARF, if physicians in the emergency department (ED) could prescribe oral NAC optionally (i.e. physician dependently) in patients with ARF who should perform enhanced CT scan in the ED. To investigate the effect of oral NAC on RCIN, we conducted a retrospective study.

Materials and methods

This study was a retrospective study based on data derived from electronic medical chart reviews. This study was conducted in the ED of an 1600-bed academic urban tertiary-care hospital with an annual ED census of 45,000 patients. From January 2006 to June 2006, Patients over 15 years who underwent enhanced CT scan in the ED were initially enrolled. Of these patients, patients with ARF with serum creatinine level>1.4 mg/dL were included for final analysis. ARF was defined as serum Cr>1.5 mg/dL. Exclusion criteria were as follows: patients of 15 years or less, with CRF or end stage renal disease.

In our hospital, we administer NAC to prevent RCIN in patients with CRF before and after CT scan. However, we do not have formal protocol in patients with ARF, and the administration of NAC is determined by each physician’s decision.

The enrolled patients were divided into the two groups: the NAC group and the control group. In the NAC group, oral NAC was given once at a dose of 600mg before CT scan and twice daily for 24 hours after CT scan. We reviewed medical records to compare the demographic characteristics, underlying diseases, current medications, we also compared volume of infused fluid, serum blood urea nitrogen and creatinine level before and after CT scan between the groups. Patients in the both groups received intravenous hydration with normal saline, Ringer’s lactate solution, dextrose, colloid or blood product according to the patients’ underlying conditions and the physician’s decisions before and after CT scan. Because of the difference in the type and volume of fluid, we calculated the total volume of various fluids during 6 hours before CT scan and 6 hours after CT scan, respectively. All patients who underwent CT scan received a nonionic, low-osmolality radiocontrast agent (Ultravist 370, Schering) intravenously.

We defined RCIN as an increase in serum creatinine level of at least 0.5 mg/dL or 25%, 48 to 72 hours after CT scan from the baseline of serum creatinine level before CT scan.

The primary outcome was the incidence of RCIN. The secondary outcome was the need for hemodialysis, mortality rate and the length of stay in hospital. Continuous variables were presented as means ± standard deviations, and Student t-test or repeated measures analysis of variance was used to compare the both groups. Categorical variables were presented as an absolute value and the percentage, and chi-square test or Fisher’s exact test as appropriate was used. A p-value of less than 0.05 was considered to be statistically significant. All statistical analyses were conducted using SAS software version 8.

Results

A total of 106 patients were included during the study period. Of those, 83 patients were in the control group and 23 patients were in the NAC group. Basic demographics were shown in Table 1. The median age was 64.2±15.4 years in the control group and 65.9±14.7 years in the NAC group (p=0.627). Age and sex were not different in the both groups. Both groups had similar underlying diseases except ischemic heart disease. In the NAC group, the number of patients with ischemic heart disease was 5 (17%), but 4 (5%) in the control