Original Article

Effect of *N*-acetyl cysteine in prevention of contrast nephropathy on patients under intravenous pyelography and contrast CT

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Abstract

Background: Contrast nephropathy is a common and often reversible cause of acute renal failure (ARF). About 10% of ARF in admitted patients might be due to it and may also lead to dialysis. Some methods could prevent it such as fluid therapy with half or normal saline, Na bicarbonate, *N*-acetyl cysteine (NAC), and so on. The aim of this study was to evaluate the efficacy of NAC to prevent contrast nephropathy.

Materials and Methods: In a cross-sectional study, 110 patients who were candidate for intravenous pyelography (IVP) or CT scan enrolled in two groups: Case and control. In patients of case group, meglumine compound and in control group, placebo was prescribed before procedure. Before study and after 48 h, blood urea nitrogen (BUN) and creatinine (Cr) was checked, and glomerular filtration rate (GFR) was measured with Cockcroft-Gault formula.

Results: There were no difference between age and gender of two groups. There was also no significant difference between mean Cr before and after study; however, GFR of patients in case group was significantly higher than the control group after 48 h of procedure.

Conclusion: Because GFR was higher in case group and there were no drug side-effects in patients, we recommend the use of NAC before administration of intravenous contrast especially in high-risk population such as diabetic patients.

Key words: Contrast CT, contrast nephropathy, intravenous pyelography, *N*-acetyl cysteine

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INTRODUCTION

Contrast-induced nephropathy (CIN) is a common and preventable cause of acute kidney injury (AKI) that is responsible for about 10% of AKI in admitted patients and it may rarely lead to dialysis.[1] Prevalence of CIN in patients with serum Cr < 1.5 mg/dl and patients with Cr > 2.5 is approximately 2% and 10%, respectively.[2] CIN has been defined as increase of 0.5 mg/dl or 25% from baseline serum creatinine.[3] Risk factors of developing CIN might be baseline chronic

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kidney disease, diabetes mellitus, multiple myeloma, congestive heart failure, decreased effective circulatory volume, advanced age, hypotension, and high dose of contrast media.[4-8] Potential causes of CIN may be hypoxia of medulla or direct toxicity of tubular epithelium. Mediators of injury are not completely known; however, changes in metabolism of angiotensin, nitric oxide, endothelin, insulin growth factor (IGF), platelet-activating factor (PAF), atrial natriutic peptide (ANP), vasodilator prostaglandins, and direct cytotoxic effect of contrast may play a role in this regard.[9,10] Contrast media can cause acute tubular necrosis and rapid increase of serum Cr during 24–48 h and then return to baseline after 5–7 days.[11] Several methods have been suggested to prevent CIN such as decreasing dose of contrast, hydration of patients with crystalloid solutions like normal saline and prescription of different drugs such as theophylline, ascorbic acid, *N*-acetyl cysteine (NAC), statins, fenoldepam, and force diuresis with loop diuretic or mannitol.[12,13] NAC has antioxidant and vasodilatory effects due to increased intracellular glutathione and serum nitric oxide, respectively.[14-16] Based on different and often controversial results of previous studies about NAC, the aim of this study was the evaluation of effect of this drug on prevention of CIN among patients under intravenous pyelography (IVP) or contrast-enhanced CT scan.

MATERIALS AND METHODS

In a comparative cross-sectional study, 110 patients who were candidate of IVP or contrast-enhanced CT were participated and randomly selected as case or control groups. Contrast agent of meglumine compound 1 ml/kg was used for all patients. While in patients of case group, NAC 600 mg/bid was prescribed from 24 h before to 24 h after procedure (total dose of 4 pearl), the patients of control group have been received placebo with the same interval and shape (both were made by Osveh Pharmaceutical Company). Hydration of case and control group patients before and after procedure was normal as previous habit. Just before and 48 h after procedure, the serum Cr of all patients were checked in the same laboratory and glomerular filtration rate (GFR) were then calculated by Cockcroft-Gault equation (GFR = age × body weight/72 × serum Cr). Increasing basal Cr more than 0.5 mg/dl or 25% of baseline were considered significant and equivalent of nephropathy. Exclusion criteria were diabetes mellitus and renal insufficiency (serum Cr ≥ 1.5 mg/dl). Obtained data were analyzed by using *t*-test, chi-square test with SPSS version 19.

RESULTS

The patients were 52 (47.3%) men and 58 (52.7%) women. Mean age of the case and control group patients were 45.4 ± 19.2 and 42.7 ± 16.8 years, respectively ($P = 0.42$). There was no significant difference between two groups in terms of gender, age, and also between systolic and diastolic blood pressure before and after the procedure ($P > 0.05$). Serum Cr increased in 5 (9.1%) and 39 (70.9%) patients of case and control groups, respectively. Inversely, serum Cr decreased in 23 (41.8%) and 4 (7.3%) patients of case and control groups, respectively ($P < 0.05$). A significant difference between values of Cr before and after procedure has been seen ($P < 0.001$) [Table 1]. After 48 h, GFR were increased in 22 (40%) and 5 (9.1%) patients and decreased in 6 (10.9%) and 40 (72.7%) patients of case and control groups, respectively, but it was unchanged in other patients.

Mean GFR and its changes have been shown in Table 2. Figures 1 and 2 can show the prevalence of Cr and GFR changes. Fortunately, complication of NAC was not found in any of patients during study.

DISCUSSION

This study has evaluated the effect of NAC in

Table 1: Mean and standard deviation of Cr in patients of two groups

Time	Group	Mean Cr	Standard deviation	*P*
Before graphy	Case	0.96	0.19	0.09
	Placebo	0.9	0.18	
After graphy	Case	0.91	0.17	0.15
	Placebo	1.12	0.21	

Table 2: Mean and standard deviation of GFR in patients of two groups

Time	Group	Mean GFR	Standard deviation	*P*
Before graphy	Case	92.2	25	0.23
	Control	86.4	25	
After graghy	Case	96	25	0.001
	Control	79.5	24	

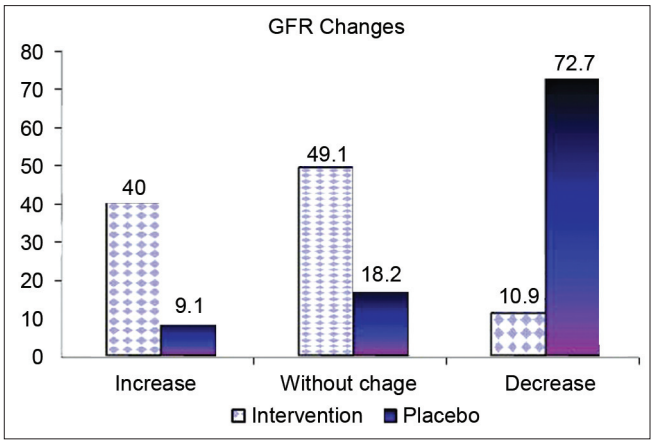

Figure 1: GFR changes in two groups

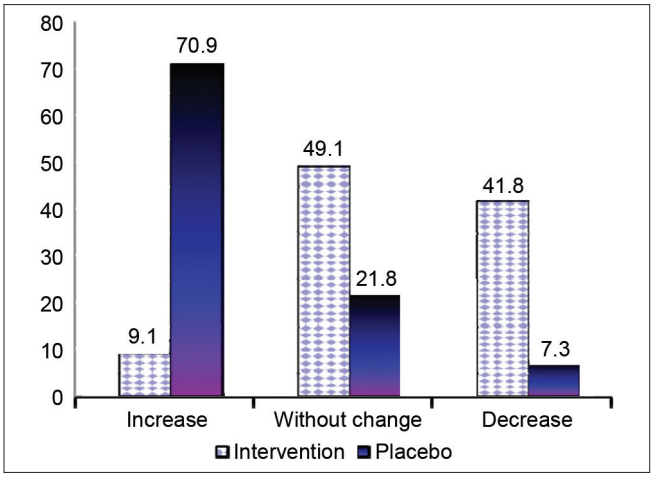

Figure 2: Cr changes in two groups

prevention of contrast nephropathy. Serum Cr before and 48 h after taking of contrast in two groups was similar in our study; however, in patients of case group, GFR was greater than control group, probably due to renoprotective effect of NAC. Discrepancy between above finding is due to this fact that same serum Cr in two patients with different age and body weight cause different GFR.

In other studies, different and sometimes controversial results have been observed; for example, in Ramesh's study on 51 patients with renal insufficiency (serum Cr > 1.5), prescription of NAC and hydration prevented from further progression of renal failure in patients under angiography.[17] In another study, on 50 patients with normal renal function, Hoffman showed that NAC 600 mg/bid can protect kidney function in patients with exposed intravenous contrast.[18] In Marenzi's study, 354 patients were enrolled in three groups: Placebo, NAC 600 mg/bid, and NAC double dose; they concluded that NAC could prevent CIN dose dependently.[19] Maloy studied on 25 chronic kidney disease patients and found that NAC could not reduced CIN.[20] Alla *et al*. evaluated 100 patients with normal renal function and showed that NAC plus normal saline compared to normal saline had better effect on prevention of CIN.[21] In a similar study, NAC was effective to prevent CIN;[22] however, in Durham's study, NAC was not effective.[23] As stated before, NAC alone or with crystalloid solution might be effective in prevention of CIN; however, in above mentioned studies, dose of NAC, duration of treatment, and dose of contrast agent were different.

Our study had some differences with these studies such as selection of patients under IVP or contrast CT with using low dose of contrast as compared with angiography, using only NAC (without crystalloid solution) with definition of the pure effect of NAC, and evaluation of patients based on GFR in addition to serum Cr in order to increasing validity and sensitivity of the study.

CONCLUSION

Based on our results, NAC is a safe and inexpensive drug due to its association with increasing of GFR; thus, we recommend prescribing this drug, especially in patients who are at higher risk for CIN such as diabetes mellitus and chronic kidney disease.

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