ORIGINAL ARTICLE

N-acetylcysteine fails to prevent renal dysfunction and oxidative stress after noniodine contrast media administration during percutaneous coronary interventions

Hakan Buyukhatipoglu[1], Yusuf Sezen[2], Ali Yildiz[2], Memduh Bas[2], Idris Kirhan[1], Turgay Ulas[1], Mehmet Nuri Turan[1], Abdullah Taskin[3], Nurten Aksoy[3]

1 Harran University School of Medicine, Department of Internal Medicine, Sanliurfa, Turkey
2 Harran University School of Medicine, Department of Cardiology, Sanliurfa, Turkey
3 Harran University School of Medicine Department of Biochemistry, Sanliurfa, Turkey

KEY WORDS

N-acetylcysteine, contrast nephropathy, oxidative stress, total antioxidant capacity, total oxidant capacity

ABSTRACT

INTRODUCTION Oxidative stress is believed to have a role in contrast-induced nephropathy. Based on this assumption, several known antioxidants have been studied to assess their effect on nephropathy, especially N-acetylcysteine (NAC). However, its usefulness has yet to be confirmed.

OBJECTIVES We aimed to assess whether NAC has any protective effect on contrast-induced renal dysfunction, and whether NAC affects the parameters of oxidative stress in serum and urine.

PATIENTS AND METHODS Sixty patients with coronary artery disease, who were scheduled for percutaneous coronary intervention (PCI), were randomized into 2 groups: one group received 600 mg NAC intravenously and the other did not. Both groups were matched for age and gender. Before and 24 hours after the procedure, blood and urine samples were obtained to assess total oxidant capacity (TOC), total antioxidant capacity (TAC), oxidative stress index (OSI), and renal function.

RESULTS Twenty-four hours after PCI, TOC and OSI levels were significantly increased and TAC levels significantly decreased, both in serum and urine. However, we did not observe any differences in oxidative parameters between patients who received NAC and those who did not. Multivariate analyses identified no protective effect of NAC on renal function, and no effect on oxidative parameters in either serum or urine.

CONCLUSIONS In this first clinical study that determined TOC and TAC levels in both serum and urine after exposure to contrast media, NAC was not found to affect oxidant parameters or protect against contrast nephropathy, at least in patients without the risk factors for nephropathy, such as diabetes mellitus or baseline renal or cardiac dysfunction.

Correspondence to:
Assist. Prof. Hakan Buyukhatipoglu, MD, PhD, Harran Universitesi Yenisehir Kampusu, Tip Fakultesi Dekanlik Binasi Kat:3 63300, Sanliurfa, Turkey,
phone: +90-414-314-8410,
fax: +90-414-313-9615,
e-mail: buyukhatipoglu@gmail.com
Received: July 6, 2010.
Revision accepted: September 22, 2010.
Conflict of interests: none declared.
Pol Arch Med Wewn. 2010; 120 (10): 383-389

INTRODUCTION Contrast-induced nephropathy (CIN) is acute renal dysfunction that is secondary to the administration of radiocontrast media. This renal impairment is generally reversible.[1] Although the exact mechanism has not yet been clearly elucidated, 2 empirically-supported central mechanisms have been proposed: renal vasoconstriction and acute tubular injury.[2]

Acute tubular injury is due either to direct cytotoxic effects, or is associated with the generation of oxygen free radicals, which cause oxidative damage.[3,4] Based on the assumption that reactive oxygen species (ROS) might be involved in the pathogenesis of CIN, numerous studies have been conducted to assess the effects of antioxidants such as N-acetylcysteine (NAC). However, clinical trials and meta-analyses that examined the effectiveness of NAC in the prevention of contrast nephropathy have provided conflicting results.[5,6]

In this pilot study, we attempted to clarify the above issues. Therefore, we examined patients who underwent elective percutaneous coronary intervention (PCI) and received at least a certain amount of contrast media; we also assessed oxidative stress using a more valid and reliable method that measured total oxidant capacity (TOC) and total antioxidant capacity (TAC) both in serum and urine. Finally, we assessed the effect of NAC administration on both renal function and oxidative parameters, again in serum and urine.

PATIENTS AND METHODS

Subjects The study was conducted at the Harran University School of Medicine, Sanliurfa, Turkey. Prior to subject recruitment, the study protocol was reviewed and approved by the university ethics committee, in accordance with the ethical principles for human investigations, as outlined by the Second Declaration of Helsinki. We recruited 60 age- and gender-matched patients with coronary artery disease (CAD) who were scheduled for and ultimately underwent PCI (according to prior coronary angiography results). All subjects gave written, informed consent prior to the study. Their baseline and demographic characteristics are shown in TABLE 1.

The exclusion criteria were as follows: acute coronary syndrome; any coexisting cardiac disease; any evidence of liver, kidney, or respiratory disease; diabetes mellitus; malignancy; any infectious, inflammatory, or infiltrative disorder; unregulated hypertension; reduced left ventricular ejection fraction, or any findings or history of congestive heart failure; recent use (within 48 h) of any drug with antioxidant properties; regular alcohol use or alcohol use within the previous 48 hours.

Study design Sixty age- and gender-matched patients with CAD were randomized into 2 groups. Just before the PCI and 24 hours after the procedure, blood and urine samples were obtained to measure TOC, TAC, and the oxidative stress index (OSI). After the baseline blood samples were obtained and just before the PCI, the first group was given 600 mg intravenous NAC.

As a contrast material, nonionic contrast media was used in various quantities (70–400 cc) depending on the clinical indications (Xenetix 300; Guerbet, Roissy, France, contains Iobitridol in 300 mg iodine/ml concentration). Adequate hydration was ensured before the procedure by advising all patients to drink at least 1500 ml of water during the preceding 24 hours. In addition, just before the procedure, each patient was given 500 cc isotonic saline. After the procedure, patients again were hydrated to ensure at least 2000 cc urine output. At 24 hour, blood and urine samples were obtained again to measure serum TOC, TAC, OSI, creatinine, and urea. Acute renal injury was defined according to the modified RIFLE criteria (Acute Kidney Injury Network), as any of the following: an abrupt absolute increase in serum creatinine of 0.3 mg/dl from baseline, an increase in serum creatinine concentration of at least 50%, or oliguria of less than 0.5 ml/kg/h for more than 6 hours.

Assays All blood samples were drawn from a large antecubital vein without interruption of venous flow, using a 19-gauge butterfly needle connected to a plastic syringe. Twenty milliliters of blood were drawn, with the first few milliliters discarded. Ten milliliters were used for baseline routine laboratory tests. The residual content of

TABLE 1 Demographic characteristics of subjects who received and who did not receive N-acetylcysteine

Variable	NAC (+)	NAC (–)	*P*
age, y	58.9 ±11.1	61.8 ±10.03	0.88
men/women	21/9	21/9	
glucose, mg/dl	96.3 ±12.1	90.8 ±14.7	0.125
SBP, mmHg	127.16 ±15.18	133.12 ±17.8	0.163
DBP, mmHg	80.33 ±10.16	82.03 ±11.6	0.545
TC, mg/dl	177.6 ±38.4	171.9 ±40.9	0.574
HDL-C, mg/dl	32.8 ±5.8	32.6 ±10.4	0.949
LDL-C, mg/dl	102.5 ±33.2	108.2 ±32.8	0.509
triglycerides, mg/dl	178.8 ±80.4	165.7 ±56.3	0.047
uric acid	4.61 ±1.66	4.98 ±1.78	0.102
sodium, mEq/l	138.6 ±2.8	138.0 ±2.9	0.707
potassium, mEq/l	4.15 ±0.44	4.37 ±0.48	0.71
calcium, mg/dl	9.6 ±0.94	9.6 ±0.99	0.982
phosphorus, mg/dl	3.14 ±0.60	3.36 ±0.64	0.184
hemoglobin, mg/dl	13.6 ±1.63	13.59 ±2.03	0.960
creatinine, mg/dl	0.89 ±0.21	0.92 ±0.25	0.373
urea, mg/dl	37.3 ±16.0	35.1 ±11.0	0.093

Abbreviations: DBP – diastolic blood pressure, HDL-C – high-density lipoprotein cholesterol, LDL-C – low-density lipoprotein cholesterol, NAC – N-acetylcysteine, SBP – systolic blood pressure, TC – total cholesterol

the syringe was transferred immediately to polypropylene tubes, which were then centrifuged at 3000 rpm for 10 minutes at 10 to 18°C. Supernatant plasma samples were stored in plastic tubes at –80°C until assayed. For the serum markers of oxidant stress, TOC was measured and the OSI calculated. TAC was measured as an indicator of antioxidant status.

Measurement of total oxidant capacity Serum TOC was measured using a novel automated method developed by Erel.[7] Oxidants present in the sample oxidize the ferrous ion-o-dianisidine complex to ferric ion. The oxidation reaction is enhanced by glycerol molecules, which are abundant in the reaction medium. The ferric ion generates a colored complex with Xylenol Orange in an acidic medium. Color intensity, which can be measured spectrophotometrically, is related to the quantity of oxidant molecules present in the sample. The assay is calibrated with hydrogen peroxide and the results expressed in terms of micro-molar hydrogen peroxide equivalents per liter (μmol H_2O_2 equiv./l).

Measurement of total antioxidant capacity Serum TAC was measured using a novel automated method developed by Erel.[8] In this method, hydroxyl radical, the most potent biological radical, is produced. In the assay, ferrous ion solution in reagent 1 is mixed with hydrogen peroxide present in reagent 2. Sequentially-produced radicals, such as the brown-colored dianisidinyl radical cation produced by the hydroxyl radical, are also potent radicals. This method allows to measure the antioxidative effect of the sample against potent free-radical reactions that are initiated by the hydroxyl radical. The assay has excellent precision values of more than 97%. The results are expressed as mmol Trolox equiv./l.

Oxidative stress index The OSI was defined as the ratio of the TOC to TAC levels. For the calculation, TAS units were changed to mmol/l and the OSI value calculated according to the following formula[7,8]:

$$\text{OSI (arbitrary unit)} = \text{TOS (}\mu\text{mol } H_2O_2 \text{ equiv./l)} / \text{TAS (mmol Trolox equiv./l)}$$

Other variables Serum sodium (Na), potassium (K), urea, creatinine, fasting blood sugar, aspartate aminotransferase (AST), alanine aminotransferase (ALT), uric acid, triglycerides, total cholesterol, high-density and low-density lipoprotein cholesterol levels were determined using the commercially-available assay kits (Abbott®, Illinois, United States) with an auto-analyser (Aeroset®, Germany).

Statistical analysis Data analysis was conducted using SPSS version 11.5 (SPSS Inc., Chicago, IL, United States) with group parameters expressed as means ± standard deviations. Between-group comparisons were made using independent-sample t-tests, and inter-group comparisons were conducted by paired-sample t-tests. The Pearson's correlation analysis was performed to identify the degree of correlation between continuous variables. Multivariate linear and logistic regression analyses were performed to identify independent predictors of renal dysfunction and oxidative stress. Differences at $P \leq 0.05$ were interpreted as statistically significant. All inferential tests were 2-tailed.

RESULTS In the whole studied population, serum TAC and OSI were significantly increased 24 hours after the PCI in both serum ($P < 0.0001$) and urine ($P < 0.0001$) (TABLE 2). TAC in serum and urine was significantly reduced after 24 hours ($P < 0.0001$ and $P = 0.006$, respectively). Serum urea and creatinine levels increased in 44 of 60 patients (73%); however, only 2 patients (3%) developed acute renal failure. Of these 2 patients, only 1 received NAC. In 16 patients (27%), creatinine and urea levels decreased.

When we compared patients who received NAC with those who did not, no statistically significant differences were observed, either pre- or post-PCI, in any of the oxidative stress parameters, or in serum urea or creatinine ($P > 0.05$ for all comparisons) (TABLE 3). Similarly, no pre- or post-PCI oxidative parameters were different in urine ($P > 0.05$ for all comparisons). No significant correlations were observed between oxidative stress parameters and creatinine or urea levels in either serum or urine; 24 hours after the procedure no significant change was observed in serum electrolytes (Na, K) and serum AST, ALT, and uric acid levels.

In a linear regression model with creatinine as a dependent variable, and serum and urine TOC and TAC, NAC, and contrast medium as independent variables, only contrast medium was found to affect creatinine levels. For the whole model, the adjusted R^2 was 0.262 ($P = 0.038$). In another model, in which an increase in creatinine levels (Δ creatinine) was a dependent variable, and NAC, changes in serum and urine TOC and TAC, and the quantity of contrast medium were independent variables, no effect on Δ creatinine was observed ($r = 0.344$, adjusted $R^2 = 0.04$, $P = 0.45$) (TABLE 3, model 2).

In another model, NAC had no effect on serum TOC; contrast medium was the only independent variable affecting TOC (TABLE 3, model 3). With serum TAC as the dependent variable, once again only contrast medium was found to alter TAC levels (TABLE 3, model 4), and NAC had no effect. Contrast media was the only significant determinant of urine TOC and TAC; NAC again had no effect on these parameters (TABLE 3, models 5 and 6).

DISCUSSION Our study provided important new insight and data. First, it differed from

TABLE 2 Serum and urine oxidative stress markers before and after percutaneous coronary intervention

Serum	Serum values, n = 60		Pre-PCI serum values		Post-PCI serum values	
	pre-PCI	post-PCI	NAC (+) n = 30	NAC (–) n = 30	NAC (+) n = 30	NAC (–) n = 30
TOC, mmol Trolox equiv./l	14.47 ±3.94[a]	19.63 ±5.60[a]	15.35 ±4.30	13.80 ±3.64	18.90 ±5.58	20.38 ±5.58
TAC, μmol H_2O_2 equiv./l	0.86 ±0.13[a]	0.79 ±0.09[a]	0.88 ±0.12	0.84 ±0.14	0.81 ±0.07	0.77 ±0.09
OSI, arbitrary unit	1.70 ±0.51[a]	2.5 ±0.77[a]	1.76 ±0.50	1.66 ±0.53	2.33 ±0.70	2.68 ±0.81
creatinine, mg/dl	0.91 ±0.23[a]	1.00 ±0.22[a]	0.92 ±0.25	0.89 ±0.21	1.11 ±0.27	0.98 ±0.26
urea, mg/dl	36.4 ±13.9[a]	42.3 ±14.09[a]	37.3 ±16.0	35.1 ±11.0	43.7 ±16.7	41.5 ±10.5
Urine	**Urine values, n = 60**		**Pre-PCI urine values**		**Post-PCI urine values, n = 30**	
	pre-PCI	post-PCI	NAC (+) n = 30	NAC (–) n = 30	NAC (+) n = 30	NAC (–) n = 30
TOC, mmol Trolox equiv./l	20.26 ±6.6[a]	29.14 ±8.54[a]	21.02 ±7.17	19.46 ±5.96	29.27 ±7.99	28.99 ±9.23
TAC, μmol H_2O_2 equiv./l	1.54 ±0.07[a]	1.48 ±0.13[a]	1.56 ±0.12	1.52 ±0.10	1.49 ±0.10	1.47 ±0.16
OSI, arbitrary unit	1.31 ±0.44[b]	1.97 ±0.60[b]	1.34 ±0.47	1.30 ±0.42	1.96 ±0.53	1.98 ±0.67

a $P < 0.0001$, **b** $P = 0.006$

Abbreviations: OSI – oxidative stress index, PCI – percutaneous coronary intervention, TAC – total antioxidant capacity, TOC – total oxidant capacity, others – see **TABLE 1**

TABLE 3 Results of regression analyses

Regression models	Dependent variables	Independent variables	β coefficient	t	*P*
model 1	creatinine	serum TOC	–0.232	2.039	0.091
		serum TAC	0.177	1.561	0.122
		urine TOC	–0.103	-0.800	0.426
		urine TAC	0.192	0.743	0.460
		NAC use	–0.148	–1.355	0.179
		contrast use	0.431	3.13	0.002
model 2	Δ creatinine	Δ TOC (serum)	0.171	0.439	0.663
		Δ TAC (serum)	0.273	1.11	0.274
		Δ TOC (urine)	0.213	2.71	0.118
		Δ TAC (urine)	0.301	1.77	0.076
		contrast amount	0.213	0.371	0.712
		NAC use	0.305	1,877	0.068
model 3	serum TOC	contrast use	0.579	6.56	0.0001
		NAC use	0.160	0.684	0.496
model 4	serum TAC	contrast use	–0.264	–2.588	0.011
		NAC use	0.210	2.055	0.063
model 5	urine TOC	contrast use	0.478	5.12	0.0001
		NAC use	0.360	1.77	0.111
model 6	urine TAC	contrast use	–0.302	–2.43	0.031
		NAC use	0.299	1.44	0.217

Abbreviations: see **TABLES 1** and **2**

the previous studies in that it assessed oxidative stress parameters using a more reliable method that measured both TOC and TAC.[7,8] Measuring different oxidant and antioxidant molecules is impractical, and their oxidant and antioxidant effects are additive. Since there are numerous oxidants and antioxidants in the body, measuring total oxidant-antioxidant status is more valid and reliable.[7,8] When only a few parameters are measured, their levels may be unchanged or decreased, even when the actual oxidant status is increased, or vice versa.

Second, in addition to serum levels, we measured oxidative status in urine samples. This is also important because the kidneys are often impaired in contrast-medium toxicity.

Free radicals and oxidants are produced in metabolic and physiological processes, and their effects are controlled by exogenous and endogenous antioxidants. If the quantity of free radicals

exceeds the capacity of anti-oxidant defense mechanisms, oxidative stress occurs.[9,10] As mentioned above, oxidative stress has been thought to play a role in acute tubular injury,[3,4] as suggested by several experimental studies[11-14] that examined various separate ROS. However, only a few clinical studies assessing oxidative stress induced by contrast medium have been conducted in humans.[15,16] Contrary to previous studies, our pilot study provided clinical data on this issue.

Numerous studies have focused on the effects of antioxidants on contrast nephropathy. The most commonly used agent as an antioxidant is NAC because it is well tolerated and inexpensive. However, its prophylactic effectiveness continues to raise controversies and its use has not yet been fully validated. Shyu et al.[17] studied patients with chronic renal insufficiency who had undergone coronary bypass surgery and found that NAC combined with adequate hydration reduced acute renal nephropathy. Likewise, Kay et al.[18] reported that NAC protected patients with moderate chronic renal insufficiency. On the other hand, Durham et al.[19] and Webb et al.[20] observed no beneficial effects of NAC in the prevention of contrast nephropathy in patients with chronic renal failure. Coyle et al.[21] studied the effects of NAC in patients with diabetes undergoing coronary angiography and showed no additional beneficial effect of NAC compared with adequate hydration alone.

There may be several reasons for the above discrepancies, including differences in baseline risk factors for acute renal failure (e.g., diabetes, baseline renal function, cardiac dysfunction, etc), the adequacy of hydration, the quantity and type of contrast medium, and the way by which contrast nephropathy was defined. Another crucial point is that these studies were designed based on the concept that the oxidant effects of contrast media play a role in the development of contrast nephropathy; therefore, an antioxidant such as NAC should protect against these effects and thus prevent nephropathy. However, these studies failed to assess oxidant or antioxidant parameters, or the causal relationship between contrast medium and oxidative parameters. In other words, contrast medium may cause oxidative stress or ROS, but whether increased oxidative stress affects renal function or not remains unclear, i.e., contrast medium might be the only factor causing renal function impairment, with ROS as a consequence rather than a cause.

In line with these results, we believe that our pilot study provides additional important data. First, our study groups were quite homogenous. To avoid confusion related to nephropathy risk factors, we excluded patients with diabetes, cardiac dysfunction, or any baseline renal impairment. All patients were adequately hydrated. We also took into consideration elevations in creatinine levels and, unlike prior studies, did not require that the full criteria for contrast nephropathy be met. Because we primarily sought to identify any causal relationship between ROS and changes in serum creatinine levels, we assumed that in the presence of adequate hydration any increase in serum creatinine levels was important. Previous studies that assessed contrast nephropathy as a bivariate variable (present or absent) may have missed contrast medium-induced renal damage that failed to reach the degree of acute renal failure, thus underestimating negative effects. Moreover, how acute renal failure is defined remains an issue of debate. Assessing any quantitative decrease in renal function is more objective. Furthermore, we assessed oxidant and antioxidant parameters both in serum and urine. In this way, the parameters measured in one confirmed and strengthened the results obtained in the other.

We observed that oxidative stress was significantly increased and antioxidant capacity significantly decreased after the use of contrast medium. However, no differences were observed between patients who received NAC vs. those who did not. More importantly, in multivariate analyses, the only factor contributing to renal function was contrast medium, and we detected no causative effect of NAC either on oxidant or antioxidant status, either in serum or urine. This suggests that NAC, as an antioxidant, does not have any protective effect. This observation is further proved by the fact that NAC did not have effects on creatinine levels either in serum or urine. Another interesting finding was that the quantity of contrast medium also did not affect creatinine levels or oxidant parameters, suggesting that there may be no dose-dependent effect of contrast media.

Our study has several limitations. First, the sample size was not large, but on the other hand, our results were strongly significant, the study groups were quite homogenous, and we analyzed parameters both in serum and urine, which made the results more reliable. Second, the subjects were not exposed to the same quantity of contrast medium, because a range of procedures was performed.

Our results can be summarized as follows: in response to contrast media, TOC levels increased and TAC levels decreased, both in serum and urine, and TOC and TAC levels were first demonstrated clinically both in serum and urine; contrast media was the only determinant of increased oxidative stress, although it was not dose-dependent; NAC had no effect on serum or urine parameters of oxidative stress; NAC had no effect on renal functions. In conclusion, oxidative stress does not seem to be a causative factor in renal dysfunction (an increase in urea and creatinine levels), and NAC seem to have no protective effects, at least in patients with normal baseline cardiac and renal function.

REFERENCES

1 Barrett BJ. Contrast nephrotoxicity. J Am Soc Nephrol. 1994; 5: 125-137.

2 Persson PB, Hansell P, Liss P. Pathophysiology of contrast medium-induced nephropathy. Kidney Int. 2005; 68: 14-22.

3 Rudnick MR, Goldfarb S, Wexler L, et al. Nephrotoxicity of ionic and nonionic contrast media in 1196 patients: a randomized trial. The Iohexol Cooperative Study. Kidney Int. 1995; 47: 254-261.

4 Heinrich MC, Kuhlmann MK, Grgic A, et al. Cytotoxic effects of ionic high-osmolar, nonionic monomeric, and nonionic iso-osmolar dimeric iodinated contrast media on renal tubular cells in vitro. Radiology. 2005; 235: 843-849.

5 Kshirsagar AV, Poole C, Mottl A, et al. N-acetylcysteine for the prevention of radiocontrast induced nephropathy: a meta-analysis of prospective controlled trials. J Am Soc Nephrol. 2004; 15: 761-769.

6 Fishbane S. N-acetylcysteine in the prevention of contrast-induced nephropathy. Clin J Am Soc Nephrol. 2008; 3: 281-287.

7 Erel O. A new automated colorimetric method for measuring total oxidant status. Clin Biochem. 2005; 38: 1103-1111.

8 Erel O. A novel automated method to measure total antioxidant response against potent free radical reactions. Clin Biochem. 2004; 37: 112-119.

9 Halliwell B, Guttridge JM. Lipid peroxidation, oxygen radicals, cell damage, and antioxidant therapy. Lancet. 1984; 1: 1396-1397.

10 Halliwell B. Free radicals, antioxidants, and human disease: curiosity, cause, or consequence. Lancet. 1994; 344: 721-724.

11 Bakris GL, Lass N, Gaber AO, et al. Radiocontrast medium-induced declines in renal function: a role for oxygen free radicals. Am J Physiol. 1990; 258: F115-F120.

12 Devrim E, Cetin M, Namuslu M, et al. Oxidant stress due to non ionic low osmolar contrast medium in rat kidney. Indian J Med Res. 2009; 130: 433-436.

13 Zager RA, Johnson AC, Hanson SY. Radiographic contrast media-induced tubular injury: evaluation of oxidant stress and plasma membrane integrity. Kidney Int. 2003; 64: 128-139.

14 Hizoh I, Haller C. Radiocontrast-induced renal tubular cell apoptosis: hypertonic versus oxidative stress. Invest Radiol. 2002; 37: 428-434.

15 Katholi RE, Woods WT Jr, Taylor GJ, et al. Oxygen free radicals and contrast nephropathy. Am J Kidney Dis. 1998; 32: 64-71.

16 Rajbala, Sane AS, Upadhyay AR, et al. Iodinated contrast media induced oxidative stress in patients undergoing urography. Panminerva Med. 2000; 42: 119-122.

17 Shyu KG, Cheng JJ, Kuan P. Acetylcysteine protects against acute renal damage in patients with abnormal renal function undergoing a coronary procedure. J Am Coll Cardiol. 2002; 40: 1383-1388.

18 Kay J, Chow WH, Chan TM, et al. Acetylcysteine for prevention of acute deterioration of renal function following elective coronary angiography and intervention: a randomized controlled trial. JAMA. 2003; 289: 553-558.

19 Durham JD, Caputo C, Dokko J, et al. A randomized controlled trial of N-acetylcysteine to prevent contrast nephropathy in cardiac angiography. Kidney Int. 2002; 62: 2202-2207.

20 Webb JG, Pate GE, Humphries KH, et al. A randomized controlled trial of intravenous N-acetylcysteine for the prevention of contrast-induced nephropathy after cardiac catheterization: lack of effect. Am Heart J. 2004; 148: 422-429.

21 Coyle LC, Rodriguez A, Jeschke RE, et al. Acetylcysteine In Diabetes (AID): a randomized study of acetylcysteine for the prevention of contrast nephropathy in diabetics. Am Heart J. 2006; 151: 1039.e9-12.

ARTYKUŁ ORYGINALNY

N-acetylocysteina nie zapobiega wystąpieniu dysfunkcji nerek i stresu oksydacyjnego po podaniu niejodowego środka kontrastowego w trakcie przezskórnej interwencji wieńcowej

Hakan Buyukhatipoglu[1], Yusuf Sezen[2], Ali Yildiz[2], Memduh Bas[2], Idris Kirhan[1], Turgay Ulas[1], Mehmet Nuri Turan[1], Abdullah Taskin[3], Nurten Aksoy[3]

1 Harran University School of Medicine, Department of Internal Medicine, Sanliurfa, Turcja
2 Harran University School of Medicine, Department of Cardiology, Sanliurfa, Turcja
3 Harran University School of Medicine Department of Biochemistry, Sanliurfa, Turcja

SŁOWA KLUCZOWE

całkowita pojemność antyoksydacyjna, całkowita pojemność oksydacyjna, N-acetylocysteina, nefropatia kontrastowa, stres oksydacyjny

STRESZCZENIE

WPROWADZENIE Uważa się, że stres oksydacyjny odgrywa rolę w nefropatii indukowanej przez środki cieniujące. Było to podstawą badań kilku znanych antyoksydantów, w szczególności N-acetylocysteiny (NAC), w celu zapobiegania nefropatii. Przydatność NAC nadal jednak wymaga potwierdzenia.

CELE Celem badania bylo ustalenie, czy NAC chroni przed dysfunkcją nerek indukowaną kontrastem oraz czy wpływa na parametry stresu oksydacyjnego w surowicy krwi i moczu.

PACJENCI I METODY Sześćdziesięciu pacjentów z chorobą niedokrwienną serca, u których zaplanowano zabieg przezskórnej interwencji wieńcowej (*percutaneous coronary intervention* – PCI), zrandomizowano do dwóch grup zgodnych pod względem wieku i płci: chorym w jednej grupie podano dożylnie 600 mg NAC, w drugiej grupie leku nie podano. Przed zabiegiem oraz 24 godziny po zabiegu pobrano próbki krwi i moczu w celu oznaczenia całkowitej pojemności oksydacyjnej (*total oxidant capacity* – TOC), antyoksydacyjnej (*total antioxidant capacity* – TAC), wskaźnika stresu oksydacyjnego (*oxidative stress index* – OSI) oraz czynności nerek.

WYNIKI Wykazano, że 24 godziny po PCI wartości TOC i OSI były istotnie większe, a TAC istotnie mniejsze zarówno w surowicy, jak i w moczu. Nie stwierdzono jednak różnic w zakresie parametrów oksydacyjnych pomiędzy chorymi, którym podano NAC, a tymi, którym go nie podano. W analizie wieloczynnikowej nie wykazano efektu ochronnego NAC na czynność nerek ani wpływu na parametry oksydacyjne w surowicy i moczu.

WNIOSKI W tym pierwszym klinicznym badaniu oceniającym poziom TOC i TAC w surowicy i moczu po ekspozycji na środki kontrastowe nie wykazano wpływu NAC na parametry oksydacyjne oraz ochrony przeciwko wystąpieniu nefropatii kontrastowej u chorych bez czynników ryzyka nefropatii takich jak cukrzyca, dysfunkcja nerek lub serca.

Adres do korespondencji:
Assist. Prof. Hakan Buyukhatipoglu, MD, PhD, Harran Universitesi Yenisehir Kampusu, Tip Fakultesi Dekanlik Binasi Kat:3 63300, Sanliurfa, Turcja,
tel.: +90-414-314-8410,
fax: +90-414-313-9615,
e-mail: buyukhatipoglu@gmail.com
Praca wpłynęła: 06.07.2010.
Przyjęta do druku: 22.09.2010.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2010; 120 (10): 383-389
Tłumaczyła dr med. Małgorzata Kolcz