

Effectiveness of Acetylcysteine on Preventing Renal Dysfunction in Patients Undergoing Coronary Procedures

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ABSTRACT

Objective: Experimental studies have shown that acetylcysteine is beneficial in preserving kidney function during coronary procedures. However, its role in routine clinical practice is not known.

Methods: We studied 75 consecutive patients undergoing coronary procedures who received acetylcysteine, and compared them with 56 consecutive similar patients who served as control. All patients had renal dysfunction, and a single operator did all procedures.

Results: Patients in the acetylcysteine group had a decrease in serum creatinine of 0.1 ± 0.3 mg/dl versus a rise of 0.2 ± 0.6 mg/dl in the control group ($P < 0.001$). When the benefit in the active drug group was correlated with baseline creatinine, it occurred in all patients, regardless of the degree of kidney dysfunction.

Conclusion: We conclude that in patients with varying degrees of renal dysfunction who undergo coronary procedures, acetylcysteine should be used in addition to hydration. It should be an accepted clinical practice that should be adopted routinely in the cardiac catheterization laboratory.

INTRODUCTION

Chronic renal insufficiency is frequently encountered in coronary artery disease patients requiring coronary angiography and is an independent marker for the severity of coronary artery disease.¹⁻³ Furthermore, renal dysfunction is an independent risk factor for

post-procedural complications and mortality.^{4,5} When dealing with such patients in clinical practice, we have to balance the benefit of accessing coronary disease with the risk of worsening kidney function in some patients. A variety of measures are usually adapted to preserve renal function. Acetylcysteine, a drug used for treating acetaminophen toxicity, has antioxidant properties. Because of that, it was thought it might prevent contrast nephropathy. In a prospective study of 63 patients with chronic renal insufficiency, acetylcysteine administration in the peri-procedural period prevented the reduction in kidney function.⁶ We instituted such a regimen in our practice 2 years ago.

The purpose of this study is to see whether instituting such a practice in a routine clinical setting results in a similar outcome. We thus report the change in the kidney function when acetylcysteine therapy is utilized, compared to a control group that only received hydration and general measures for the prevention of contrast nephropathy.

MATERIALS AND METHODS

All patients who underwent coronary angiography and/or intervention between July 2000 and August 2002 were reviewed. Patients with chronic renal failure were identified from the electronic medical records. No patients were excluded from the analysis in either group. The use of acetylcysteine was adjudicated by review of the original records, as well as the creatinine before and after the procedure. The preoperative creatinine was obtained using the routine preoperative kidney function assessment obtained 1-7 days before the procedure. These data were compared with the data obtained for cases done January 1999-June 2000, where only general measures were utilized, and before instituting the acetylcysteine protocol. Acetylcysteine was used in a dose of 600 mg po 1 hr prior to the procedure and a second dose the evening of the procedure. The research regulatory office and the institutional review

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board approved the protocol prior to data collection. To avoid the bias of multiple operative technique variability, a single operator did all the cases in the active treatment group and control group. The single operator was a prerequisite to make sure that the same technique was utilized in both the study and the control group. The generally accepted practices of maintaining good hydration and minimizing the amount of dye were observed for all patients.

STATISTICAL METHODS

Descriptive analyses are presented by group and include the mean, standard deviation, range for age, laboratory results, and the frequency and percent by gender. Post-procedure laboratory results were compared after the adjustment for baseline by 2 standard statistical methods. First, paired differences were compared among groups using the Wilcoxon Rank-sum test. Secondly, analysis of covariance was used to model the post-procedure creatinine based upon the group and baseline creatinine. This statistical model was fit after logarithmic transformation and restriction to a baseline range of 1.2–2.9 mg/dl, common to both groups. Residuals from the model were analyzed to verify that the model fit the data well. A *P*-value <0.05 was considered significant.

RESULTS

Seventy-five patients were identified in the acetylcysteine group and 56 in the control group. There was no significant difference between the 2 groups in baseline characteristics (Table 1). All patients received the general measures of hydration and biplane cineangiography using only minimal amounts of iodine dye, if at all possible. Post-angiography BUN and creatinine were higher in the control group, while they decreased in the acetylcysteine group. The difference was consistent and in favor of the acetylcysteine group (Table 2). In the acetylcysteine group, the creatinine clearance improved following angiography by 5.3 ± 13.0 ml/min. While the rise in serum creatinine in the control group was correlated with baseline creatinine (the worse the baseline, the greater rise in creatinine was noted), the benefit in the acetylcysteine group was not correlated with the baseline creatinine (Figure 1).

DISCUSSION

Patients with renal dysfunction present a real challenge to the invasive and interventional cardiologist. The occurrence of contrast nephropathy ranges be-

Table 1. Baseline Characteristics

Variable	Acetylcysteine Group (n=75)	Control Group (n=56)	P
Age	70.2 ± 11.4 years	72.2 ± 9.5 years	N.S.*
Male sex	64.0%	67.9%	N.S.
Baseline BUN	30.3 ± 10.5 mg/dl	28.2 ± 12.5 mg/dl	N.S.
Baseline creatinine	1.5 ± 0.3 mg/dl	1.7 ± 0.9 mg/dl	N.S.

*N.S.=not significant

Table 2. Change in BUN and Creatinine Following Angiography

	Acetylcysteine	Control
BUN change*	-1.8 ± 6.8 mg/dl† (range -26 to +13)	3.0 ± 8.2 mg/dl (range -16 to +36)
Creatinine change	-0.1 ± 0.3 mg/dl‡ (range -0.7 to +0.8)	0.2 ± 0.6 mg/dl (range -0.3 to 3.2) *

* Acetylcysteine versus control (Wilcoxon test)

† *P* = 0.001

‡ *P* <0.001

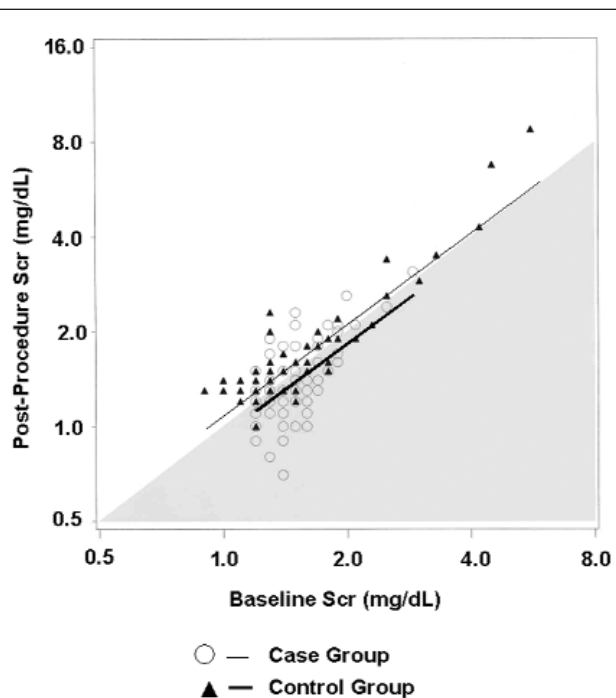


Figure 1. Correlation between post-procedural creatinine and baseline serum creatinine in the acetylcysteine group (open circle) and control group (triangle). Patients in the acetylcysteine group had a decrease in creatinine values, while the control group had an increase (*P*<0.001 Wilcoxon test). While control post-procedure values correlated well with baseline (correlation 0.3 by Spearman correlation), there was no correlation in the treatment group and no specific pattern, suggesting a benefit for the drug regardless of baseline creatinine.

tween 5% in patients with mild renal dysfunction to 50% in those with significant kidney disease.⁷ Since the factors that predispose people to coronary artery disease are similar to those that lead to renal dysfunction, it is not surprising that more than one-third of patients with acute coronary syndromes who undergo coronary angiography have preexisting renal dysfunction.⁸ The problem is compounded by the fact that each of these patients may require repeat procedures. With a decline in kidney function, every subsequent procedure may exacerbate renal dysfunction. Therefore renal dysfunction became a very important factor in predicting outcomes in acute coronary syndromes.

To avoid higher complication rates, the utilization of cardiac catheterizations and interventions in renal dysfunction patients is less than in those with normal function⁹ despite the increased necessity of these procedures in patients with renal dysfunction. For all of these reasons, prevention of contrast nephropathy is becoming a major priority in the cardiac catheterization laboratories. Several measures were utilized in the past to decrease the incidence and severity of contrast nephropathy. In all cases, the use of a less dye volume, non-ionic, low osmolar agent is recommended. Techniques like biplane angiography and rotational spin may help us to achieve this goal.¹⁰

Hydration is another routine general measure that should be utilized. Isotonic hydration was shown to be superior to the use of half normal saline.¹¹ Forced diuresis with mannitol has not consistently proven to be of any benefit¹² and its use is currently not in vogue. Adjunctive therapy with theophylline or dopamine had a variable result in various studies.¹³⁻¹⁷ Fenoldopam has some promise, however. In a randomized controlled study of 45 patients, the drug had augmented the renal plasma flow, yet the effect on decreasing contrast nephropathy incidence was not statistically significant.¹⁸ A recent study presented at the American College of Cardiology meeting did cast more doubt on the benefit of this drug. The use of this drug also adds a significant cost to the procedure. The need to have a medication that is simple to use, has a low cost, and consistently shows a benefit in preventing contrast nephropathy is still there. This ignited the recent interest in the use of acetylcysteine.

Contrast materials decrease medullary blood flow and exert a direct toxic effect thought to be mediated through the production of oxygen free radicals.¹⁹ Acetylcysteine may increase renal medullary blood flow and is a free-radical scavenger. Because of these

properties, it was studied in an attempt to decrease the incidence of contrast nephropathy.

In a prospective study, 83 patients undergoing computed tomography were randomized to acetylcysteine or placebo. The dose of the drug was 600 mg orally, twice daily. Acetylcysteine prevented the deterioration in renal function.⁶ Similar beneficial results were noted in patients undergoing coronary angiography.²⁰⁻²² Despite the consistency in results, the benefits are modest and only work when used with the general measures, including hydration and the use of the least necessary amount of dye. When the amount of dye exceeds 140 ml/patient, no significant benefit is to be expected.²³

In our study, acetylcysteine was beneficial in improving serum creatinine and creatinine clearance, contrary to the control group where serum creatinine deteriorated. More importantly, the benefit of acetylcysteine was not correlated with baseline kidney function and the benefit appears to be universal to all patients. In other words, acetylcysteine benefited patients with mild as well as moderate kidney dysfunction. This study suggests that the benefit shown in controlled experimental studies with this drug can be produced in real time clinical practice, and that this benefit can be elicited regardless of baseline kidney function.

STUDY LIMITATIONS

The majority of patients with renal dysfunction in our study were mild to moderate with a maximum creatinine level of 2.9 mg/dl. The benefit in a more severe form of kidney dysfunction needs further investigation.

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