Reducing Contrast-Induced Nephropathy Associated with Primary Angioplasty

Marenzi G, Assanelli E, Marana I, et al. N-acetylcysteine and contrast-induced nephropathy in primary angioplasty. N Engl J Med 2006;354:2773–82.

Study Overview

Objective. To evaluate *N*-acetylcysteine in the prevention of contrast-induced nephropathy (CIN) in patients undergoing primary angioplasty.

Design. Randomized controlled trial.

Setting and participants. 354 consecutive patients presenting with ST-segment elevation acute myocardial infarction (MI) requiring primary angioplasty at a single hospital in Milan, Italy, between 20 February 2003 and 1 May 2005 were included. Patients were randomized to 1 of 3 groups: (1) the control group (n = 119); (2) the standard-dose group (n = 116), which received 600 mg intravenous (IV) *N*-acetylcysteine bolus before angioplasty and 600 mg orally twice daily for 48 hours after angioplasty; or (3) the high-dose group (n = 119), which received 1200 mg *N*-acetylcysteine IV bolus before angioplasty and 1200 mg orally twice daily for 48 hours after angioplasty. All patients were hydrated with IV isotonic saline after primary angioplasty.

Main outcome measure. Occurrence of CIN, defined as ≥ 25% increase in serum creatinine from baseline within 72 hours after angioplasty.

Main results. Overall, 66 patients developed CIN, including 39 (33%) in control group, 17 (15%) in standard-dose group, and 10 (8%) in high-dose group (P < 0.001). Six patients (5%) in control group, 3 (3%) in standard-dose group, and 1 (1%) in high-dose group developed acute renal failure requiring dialysis (P = 0.14). Thirteen patients (11%) in the control group, 5 (4%) in standard-dose group, and 3 (3%) in the high-dose group died (P = 0.02).

Conclusion. In patients undergoing primary angioplasty for ST-segment elevation acute MI, *N*-acetylcysteine demonstrates dose-dependent prevention of CIN when given intravenously before and orally after angioplasty.

Commentary

CIN is associated with increased morbidity and mortality following percutaneous coronary intervention (PCI) [1]. In one of the largest retrospectives studies on this subject (7000 cases of PCI) Rihal and colleagues [1] showed that although incidence of CIN was only around 3%, those who developed CIN had a much higher risk of in-hospital death and up to a 50% increase in mortality at 5 years. Many other trials have demonstrated that *N*-acetylcysteine can decrease the incidence of CIN for diagnostic procedures involving radiocontrast. Recent reviews suggest that CIN can be mitigated with appropriate preprocedural risk factor optimization and the use of a low-ionic contrast agent, both of which are now current practice [2,3]. However, there is still controversy regarding what prophylactic agent should be used with each at-risk population.

Marenzi and colleagues selected patients at the highest risk for developing CIN, specifically those with an ST-segment elevation acute MI who were undergoing PCI. These patients are often not optimized preprocedure and tend to receive a much larger contrast load when compared with a diagnostic computed tomography scan or cardiac catheterization. Marenzi and colleagues were able to demonstrate that *N*-acetylcysteine administration via IV bolus infusion before the procedure and orally for 2 days postprocedure decreased the risk for developing CIN in a dose-dependent fashion. Prior studies have used oral *N*-acetylcysteine, not IV *N*-acetylcysteine, and most administered it 1 day pre- and 1 day postprocedure. Possibly, IV infusion of *N*-acetylcysteine may achieve a much higher serum concentration, thereby maximizing postulated antioxidative and vasodilatory effects.

Although the study was not powered to do so, the authors were able to demonstrate a decreased rate of in-hospital mortality and a significant trend toward decreased need for dialysis for acute renal failure and mechanical ventilation for acute respiratory failure . In addition, a trend toward decreased cardiopulmonary resuscitation and ventricular tachycardia/fibrillation was of borderline significance. It is unclear if these trends are attributable to *N*-acetylcysteine, as previous studies did not demonstrate this. However, these findings warrant further investigation in a much larger trial.

Applications for Clinical Practice

In high-risk patients undergoing primary angioplasty, *N*-acetylcysteine may prevent CIN and is potentially

associated with decreased in-hospital death.

—Review by Mark S. Horng, MD

References

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