Comparison of 3 Antioxidant Combinations for Preventing Contrast-Induced Nephrotoxicity

Briguori C, Airoldi, F, D'Andrea D, et al. Renal Insufficiency Following Contrast Media Administration Trial (REMEDIAL): a randomized comparison of 3 preventive strategies. Circulation 2007;115:1211–7.

Study Overview

Objective. To compare 3 intravenous (IV) strategies for preventing contrast-induced nephrotoxicity (CIN) in medium- to high-risk patients with chronic kidney disease.

Design. Prospective, randomized, double-blind study.

Setting and participants. Patients who underwent coronary and/or peripheral angiography and/or angioplasty at 1 of 2 institutions between January 2005 and August 2006 were eligible if they were aged ≥ 18 years and had a stable serum creatinine level ≥ 2.0 mg/dL and/or an estimated glomerular filtration rate (GFR) < 40 mL/min/1.73 m^2. GFR was calculated by applying the level-modified Modification of Diet in Renal Disease formula. Key exclusion criteria included serum creatinine levels ≥ 8 mg/dL; exposure to radiographic contrast within 2 days of the study; and a history of dialysis, acute myocardial infarction, or dopamine administration.

Intervention. Patients randomly received 1 of 3 treatments: IV saline plus *N*-acetylcysteine (saline/NAC), IV sodium bicarbonate plus NAC (bicarbonate/NAC), or IV saline plus IV ascorbic acid plus NAC (saline/ascorbic acid/NAC) before and after administration of a contrast agent. All patients were given IV isotonic saline (0.90%; an iso-osmolar, nonionic contrast agent) at a rate of 1 mL/kg body weight per hour.

Main outcome measures. The primary endpoint was development of CIN, defined as an increase of ≥ 25% in the serum creatinine concentration 48 hours after administration of contrast media or the need for dialysis. CIN was alternatively defined as an increase of ≥ 0.5 mg/dL in the serum creatinine concentration 48 hours after contrast exposure and a decrease of estimated GFR of ≥ 25% at 48 hours.

Main results. 326 of 351 patients randomized to treatment were analyzed (saline/NAC, n = 111; bicarbonate/NAC, n = 108; saline/ascorbic acid/NAC, n = 107). CIN occurred far less often in the bicarbonate/NAC group (2/108 [1.9%] patients) than in the saline/NAC group (11/111 [9.9%] patients; P = 0.019) or the saline/ascorbic acid/NAC group (11/107 [10.3%]; P = 1.00). Similarly, when defined using alternative definitions, CIN occurred less frequently in the bicarbonate/NAC group as compared with the saline/NAC and saline/ascorbic acid/NAC groups (1 patient vs. 10 patients in each group, respectively; P = 0.026).

Conclusion. Bicarbonate/NAC was superior to saline/NAC and saline/ascorbic acid/NAC for reducing CIN in medium- to high-risk patients with chronic kidney disease.

Commentary

NAC has been shown to be an effective antioxidant that may prevent CIN by improving renal hemodynamics and stopping direct oxidative tissue damage [1]. Additionally, bicarbonate [2] and ascorbic acid [3] have shown promising results for reducing CIN. Briguori and colleagues sought to determine whether a combination of these agents provides additive benefit for reducing CIN in medium- to high-risk patients with chronic kidney disease. The authors found that the combination of bicarbonate and NAC was superior to both saline/NAC and saline/ascorbic acid/NAC for preventing CIN in this patient population. The authors hypothesize that NAC and ascorbic acid may reduce CIN through similar pathways, whereas bicarbonate may work through another mechanism and be additive to NAC.

Overall, the study was methodologically sound. Inclusion criteria were clear and follow-up was performed for all patients. Relevant baseline characteristics were not different among the groups. The authors analyzed the primary endpoint of CIN using 2 definitions, both of which favored the bicarbonate/NAC strategy over the saline/NAC or saline/ascorbic acid/NAC strategy. There were a few limitations to the study. First, investigators did not test whether a strategy combining bicarbonate and ascorbic acid would be beneficial. In addition, the findings include only patients at medium to high risk of CIN and may not be generalizable to low-risk or very high-risk patients.

Applications for Clinical Practice

This study answers the question of how to reduce CIN in patients with elevated serum creatinine levels. Incidence of CIN was reduced from 9.9% to 1.9% in patients who received NAC (1200 mg twice daily, the day before and after contrast

administration) and sodium bicarbonate (154 mEq/L in dextrose and water at 3 mL/kg/hr for 1 hour prior to contrast administration and 1 mL/kg/hr during and 6 hours after contrast administration). The number needed to treat to prevent 1 episode of CIN was 12.5. Bicarbonate is relatively inexpensive and has few adverse effects, and it seems reasonable that this protocol should be considered in all patients with elevated serum creatinine levels who will be undergoing procedures with radiocontrast.

—Review by Robert L. Huang, MD

References

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