
Should Intravenous N-Acetylcysteine Be Considered Standard of Care for Prevention of Radio-Contrast–Induced Nephropathy?

Baker et al. (1) in a recent issue of the Journal reported results from the RAPPID trial, which tested the hypothesis that intravenous (IV) administration of N-acetylcysteine (NAC) with saline was superior to saline hydration alone for emergent procedures. The investigators concluded that IV NAC should be considered for all patients at risk for radiocontrast–induced nephropathy (RCIN) when time precludes oral prophylaxis. Although this trial encourages further research into the use of IV NAC for prevention of RCIN, several questions must be answered before IV NAC should be considered standard of care, particularly in the U.S.

Comparing a high-dose IV NAC regimen with hydration alone, the researchers found that the risks of RCIN were decreased in patients receiving IV NAC. These findings are similar to others utilizing oral NAC prophylaxis, although in most cases the regimen was initiated several hours prior to a planned procedure (2–4). Data evaluating the use of oral NAC immediately prior to a procedure are limited (4,5). Díaz-Sandoval et al. (4) compared oral NAC with placebo in the APART trial, reporting significant results favoring the oral NAC regimen. Durham et al. (5) did not report benefits from oral NAC 1200 mg given 1 h prior to and 3 h after a procedure when compared with placebo and hydration alone. It is unclear whether the unique oral NAC regimen or the volume of saline hydration used contributed to negative results. Inclusion of an oral NAC regimen as a comparative arm in the RAPPID trial would have been helpful in clarifying whether an IV NAC regimen offers advantages over oral administration.

Intravenous NAC is not commercially available in the U.S., and although some support the IV use of the inhalation solution for acetaminophen overdose, such regimens are infrequently used in the U.S. (6). If used, the inhalational solution should be filtered using a 0.22-μm filter to assure product sterility (7); however, U.S. products are not currently tested for pyrogens or bacterial endotoxins, which would not be removed using this process (personal communication, Bristol-Myers Squibb Company, and American Regent Laboratories, July 2003).

Dribben et al. (7) recently reported the stability of inhalational NAC when compounded in 5% dextrose (D5W). Stability data using inhalational NAC in solutions other than D5W are limited, although RAPPID investigators used saline. The rate and volume of normal saline used as the diluent in this study may have contributed to their positive findings. Clinicians using IV NAC must proactively determine whether the most widely accepted diluent in the U.S. should be used, and whether adjunctive saline hydration has the potential to increase the incidence of adverse outcomes observed in the RAPPID trial if D5W is chosen as a diluent.

Until data establishing the appropriate dose and safety of inhalational NAC administered IV are available, we recommend administration of saline hydration in conjunction with immediate initiation of oral NAC 600 mg twice daily for four doses in patients undergoing emergent procedures. This regimen appears to be safe, inexpensive, and effective for minimizing the risk of RCIN.

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REFERENCES


REPLY

We understand that intravenous (IV) N-acetylcysteine (NAC) as used in our study (Celltech Pharmaceuticals, Berkshire, SL1 3WE, United Kingdom) is not available in the U.S. We agree with Huxtable and colleagues’ concerns over the use of inhalational NAC for the prevention of radiocontrast–induced nephropathy (RCIN), particularly as this preparation requires the use of 5% dextrose as the diluent. Although a saline-induced diuresis appears to be effective in reducing the incidence of RCIN (1) there is no evidence for the efficacy or otherwise of 5% dextrose.