

# Review: Prophylactic acetylcysteine reduces contrast nephropathy in chronic renal insufficiency

Birck R, Krzossok S, Markowitz F, et al. Acetylcysteine for prevention of contrast nephropathy: meta-analysis. *Lancet*. 2003;362:598-603.

## QUESTION

In patients with chronic renal insufficiency, does prophylactic acetylcysteine with hydration reduce the incidence of contrast nephropathy more than hydration alone?

## DATA SOURCES

Studies were identified by searching (up to February 2003) MEDLINE (from 1966), BIOSIS (from 1989), Web of Science (from 1997), Current Contents Medizine, and the Cochrane Library; scanning references of relevant studies and review articles; and reviewing the proceedings from major cardiology and nephrology meetings from the past 5 years.

## STUDY SELECTION AND ASSESSMENT

Studies were selected if they were randomized, placebo-controlled trials published in any language that evaluated acetylcysteine to prevent contrast nephropathy in patients with chronic renal insufficiency receiving contrast media for diagnostic or therapeutic procedures.

## OUTCOMES

Development of contrast nephropathy (increase in serum creatinine  $\geq 44.2$   $\mu\text{mol/L}$  or 25% increase from baseline values) at 48 hours after contrast media administration.

## MAIN RESULTS

7 trials (805 patients, mean age 69 y, 57% to 90% men) met the inclusion criteria. 6 trials included patients receiving cardiovascular interventions and used intra-arterial administration of contrast dye; 1 trial used intravenous administration for elective computed tomography examinations. In 4 trials, acetylcysteine showed a reduction in contrast nephropathy, whereas in 3 trials, groups did not differ. The studies were pooled using a random-effects model because of significant

heterogeneity and showed a benefit of prophylactic acetylcysteine (Table). Meta-regression showed that the amount of radiocontrast media administered and the baseline level of chronic renal insufficiency did not affect results.

## CONCLUSION

In patients with chronic renal insufficiency, adding prophylactic acetylcysteine to hydration reduces the incidence of contrast nephropathy more than hydration alone.

*Source of funding: No external funding.*

*For correspondence: Dr. R. Birck, University Hospital Mannheim, Mannheim, Germany. E-mail rainer.birck@med5.ma.uni-heidelberg.de.* ■

## Acetylcysteine vs placebo to prevent contrast nephropathy in chronic renal insufficiency at 48 hours after procedure\*

Outcome	Weighted event rates		RRR (95% CI)	NNT (CI)
	Acetylcysteine	Placebo		
Contrast nephropathy†	7%	18%	56% (12 to 78)	10 (6 to 35)

\*Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article using a random-effects model.

†Increase in serum creatinine  $\geq 44.2$   $\mu\text{mol/L}$  or 25% increase from baseline values.

## COMMENTARY

Since the initial report in 2000 (1), prophylactic use of acetylcysteine, in combination with intravenous saline, has become the standard of care to prevent contrast nephropathy. This medication is particularly attractive because it is inexpensive and well tolerated, and no study has shown substantial toxicity associated with its use. The presumed method of action is to prevent tubular damage related to reactive oxygen molecules, although the exact mechanism of contrast nephropathy remains unclear. Just as unclear has been the true usefulness of acetylcysteine, as many studies have shown limited benefit.

Birck and colleagues have attempted to better define the efficacy of acetylcysteine, and their meta-analysis showed a benefit associated with its use. Despite the positive findings, however, the true clinically meaningful benefit of acetylcysteine remains unclear. Specifically, is a 25% increase in serum creatinine level an important enough endpoint (compared with acute renal failure requiring dialysis or prolonged hospitalization)? Also, as Birck and colleagues noted, publication bias may be present, limiting the number of negative studies available for analysis. Finally, aggressive saline hydration by itself appears to be very effective (2), but whether it adds to, or diminishes, the effects of acetylcysteine

has not been thoroughly studied.

Despite these limitations, this analysis provides the strongest reason yet to use prophylactic acetylcysteine, particularly in light of the > 50% relative risk reduction in contrast nephropathy. As a result, the present standard of care should probably include acetylcysteine, 600 mg twice per day, given the day before and the day of the procedure, with intravenous normal saline for several hours before and after radiocontrast administration. This should be done in all patients with an elevated serum creatinine level.

*Gregory K. Buller, MD  
St. Mary's Hospital  
Waterbury, Connecticut, USA*

## References

1. Tepel M, van der Giet M, Schwarzfeld C, et al. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med*. 2000;343:180-4.
2. Trivedi HS, Moore H, Nasr S, et al. A randomized prospective trial to assess the role of saline hydration on the development of contrast nephrotoxicity. *Nephron Clin Pract*. 2003;92:C29-34.