Intravenous N-acetylcysteine prevented contrast nephropathy

Baker CS, Wragg A, Kumar S, et al. **A rapid protocol for the prevention of contrast-induced renal dysfunction: the RAPPID study.** J Am Coll Cardiol. 2003;41:2114-8.

QUESTION

In patients with stable renal dysfunction, is a rapid protocol of intravenous (IV) N-acetylcysteine (NAC) more effective than prolonged IV saline hydration for preventing contrast nephropathy?

DESIGN

Randomized {allocation concealed*}†, blinded {data collectors}†,* controlled trial with 48- and 96-hour follow-up (Rapid Protocol for the Prevention of Contrast-Induced Renal Dysfunction [RAPPID] study).

SETTING

3 hospitals in London, England, UK.

PATIENTS

80 patients (mean age 69 y, 87% men) with stable renal dysfunction (serum creatinine [SCr] level > 120 µmol/L or creatinine clearance < 50 mL/min) who were having coronary angiography or coronary intervention. Exclusion criteria were acute renal failure or end-stage renal failure on dialysis, receipt of a nonsteroidal antiinflammatory agent (except for aspirin, 75 to 150 mg) within 24 hours, systolic blood pressure < 90 mm Hg, hemodynamically significant valvular heart disease, or signs of cardiac failure. {76 patients (95%) at 48 hours and 74 patients (92.5%) at 96 hours were included in the analysis}†.

INTERVENTION

Patients were allocated to rapid protocol (IV NAC, 150 mg/kg in 500 mL saline [0.9%] for 30 min immediately before contrast exposure and 50 mg/kg in 500 mL saline for the subsequent 4 h) (n = 41), or a control protocol (saline IV hydration, 1 mL/kg per h for 12 h before and after contrast exposure) (n = 39). All patients were given free oral fluids immediately after contrast exposure.

MAIN OUTCOME MEASURES

Incidence of contrast nephropathy (25% increase in SCr level) at either 48 or 96 hours after contrast administration.

MAIN RESULTS

Analysis was by intention to treat. Fewer patients in the IV NAC group developed contrast nephropathy than did those in the control group (Table). In the IV NAC group, mean SCr level decreased from baseline at 48 and 96 hours after administration of the contrast agent (Table). Adverse events occurred in 10 patients (12.5%), of whom 4 (5%; 2 patients in each group) had pulmonary edema.

CONCLUSION

In patients with stable renal dysfunction, a rapid protocol of intravenous (IV) N-acetylcysteine was more effective than prolonged IV saline hydration for preventing contrast nephropathy.

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For correspondence: Dr. C.S. Baker, Charing Cross Hospital, London, England, UK. E-mail cbaker@hhnt.org.

*See Glossary.

†Information provided by author.

Intravenous (IV) N-acetylcysteine (NAC) vs IV saline hydration (control) for preventing contrast nephropathy‡

Outcomes	IV NAC	Control	RRR (95% CI)	NNT (CI)
Incidence of contrast nephropathy at 96 h (n = 80)	4.9%	20.5%	76% (9 to 94)	7 (4 to 85)

Serum creatinine level (µmol/L)	Mean change from baseline§		Difference in mean change from baseline (CI)	P value
48 h (n = 76)	–7.34	4.21	11.5 (–1.6 to 24.7)	0.04‖
96 h (n = 74)	–7.44	8.17	15.6 (2.97 to 28.2)	0.008‖

‡Abbreviations defined in Glossary; RRR, NNT, CI, and difference in mean change from baseline calculated from data in article.
§Mean change from baseline provided by author.
‖The Wilcoxon-Mann-Whitney U test was used.

COMMENTARY

Prevention of contrast nephropathy is important for patients who are at risk because the consequences may include dialysis or death. Few preventive strategies have been proven efficacious, safe, and practical. Deliberate hydration with saline is an accepted strategy (1).

Results of several recent trials comparing oral NAC (mostly at 600 mg every 12 h for 4 doses, beginning before contrast exposure) with placebo plus saline hydration have been mixed. The weight of evidence favors the use of NAC, which is inexpensive and safe (2). The optimal dose, duration, and route of administration of NAC for the indication of contrast nephropathy have not been established. Oral regimens initiated the day before contrast exposure (as used in previous trials) pose logistic challenges for elective cases and are not applicable in emergencies.

The rapid IV NAC protocol used by Baker and colleagues showed efficacy similar to other trials using more prolonged, lower-dose oral regimens. The contrast dose used by Baker and colleagues was relatively high, but the degree of preexisting kidney impairment was only moderate. Although 1 rationale for the trial was to test a regimen applicable in emergencies, the patients were not selected from such a population. In addition, patients who were unstable because of hypotension or heart failure were excluded.

The results from this study support the growing body of evidence favoring the use of NAC and extend our knowledge of its dosage and route of administration. Costs should be favorable compared with more prolonged saline administration. The protocol tested in this trial would be most applicable to ambulatory programs for stable patients; caution should be observed in unstable patients because of the risk for pulmonary edema.

Brendan Barrett, MD
Memorial University of Newfoundland
St. John's, Newfoundland, Canada

References

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2. **Birck R, Krzossok S, Markowetz F, et al.** Lancet. 2003;362:598-603.