

■ clinical contributions

How Can We Reduce the Incidence of Contrast-Induced Acute Renal Failure?

Report of a Case

A 60-year-old female with history of diabetes mellitus type II, hypertension, coronary artery disease, and chronic kidney disease (baseline serum creatinine level 1.5 mg/dL, and GFR 38 mL/min) was admitted to the hospital with a non-ST elevation myocardial infarction. In preparation for cardiac catheterization, the patient received N-acetylcysteine (Mucomyst). She then underwent catheterization with the placement of two stents.

The next day, the patient had decreased urine output (900 mL/day). From a baseline level of 1.5 mg/dL, measured on the first hospital day, the creatinine level increased on subsequent hospital days to 2.0 mg/dL, 3.3 mg/dL, 3.8 mg/dL, and 4.9 mg/dL, respectively. Neither the patient's medical history nor review of her medical chart showed any evidence of periprocedural hypotension or use of nephrotoxic medication. Thus, this rapid onset of acute renal failure after cardiac catheterization was probably secondary to contrast-induced nephropathy. The nephrology service was then consulted for treatment of acute renal failure and for possible initiation of renal dialysis.

Contrast-Induced Nephropathy

Contrast-induced acute renal failure is defined as creatinine level increased at least 0.5 mg/dL or >25% above the baseline level. Patients are usually not oliguric and characteristically have low levels of urine sodium because of impaired ability to concentrate urine. Although described to occur within 24 to 48 hours after exposure, the renal failure usually peaks within 3-5 days after completion of the procedure and is most often self-limiting.

The incidence of contrast nephropathy varies from 5% to 38%, depending on the risk factors of the patient.^{1,2} Contrast nephropathy may account for more than 10% of hospital-acquired cases of acute renal failure, but fewer than 5% of these patients will require

dialysis.³ More commonly, serum creatinine level rises only moderately, and the clinical significance of this mild renal impairment is unclear.

The differential diagnosis of contrast-induced nephropathy includes renal atheroemboli, volume depletion, and interstitial nephritis. In most cases, onset of atheroemboli-associated renal failure occurs incrementally days to weeks after completion of the procedure. The course is more prolonged and is accompanied by little or no recovery of renal function. Physical examination may show other signs of embolic phenomena, including levido reticularis and embolic lesions. In addition, urine eosinophils and decreased complement levels may be present. Clinically, volume depletion can be distinguished from contrast-induced nephropathy. In both cases, urine electrolyte testing will show low urinary sodium levels, but documented hypotension and negative fluid balance are more suggestive of volume depletion.

The mechanism of contrast-induced nephropathy remains unclear. One theory proposes that alterations in nitric oxide metabolism lead to renal vasoconstriction and thereby cause decreased renal perfusion and acute renal failure. Another theory hypothesizes that contrast medium is directly toxic to the renal tubules. In either case, the damage may be mediated by formation of free radicals in the acidic tubular environment.

Treatment and Prevention of Contrast-Induced Nephropathy

Supportive treatment should be given until the acute renal failure resolves. As mentioned earlier, fewer than 5% of patients will require dialysis.³ Prevention is key and should focus on limiting risk factors (Table 1). A helpful approach is to opt for noncontrast studies whenever possible (ie, MRI, ultrasonography, noncontrast CT). The damage associated with contrast agents can be minimized also by using lower doses of contrast

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Table 1. Risk factors for contrast-induced acute renal failure

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|-----------------------------------|
| Creatinine level \geq 1.5 mg/dL |
| GFR \leq 60 mL/min |
| Diabetic nephropathy |
| Congestive heart failure |
| Hypovolemia |
| High doses of contrast medium |
| Multiple myeloma |

medium and by using low-osmolal or iso-osmolal non-ionic contrast agents. Iso-osmolal nonionic agents have shown the lowest incidence of contrast-induced nephropathy⁴ but are expensive and not yet in wide use.

Studies have evaluated use of vasodilators (eg, dopamine and fenoldopam) for preventing contrast-induced renal failure^{5,6} but have not shown a clinically significant decrease in contrast-induced acute renal failure in patients receiving these treatments. Other attempts at prevention—ie, use of mannitol- and furosemide-induced diuresis as well as prophylactic hemodialysis given after contrast administration—also failed to be effective.^{7,8} Recently, promising results were produced by a study⁹ of periprocedural continuous hemofiltration administered to prevent contrast-induced nephropathy, but larger studies are needed to confirm these results. Two other treatments—oral N-acetylcysteine administration and bicarbonate infusion—have received substantial attention and have also produced promising results.

Table 2. Results reported by Alonso, et al¹⁰

| Group | Incidence of radiocontrast induced nephropathy |
|------------------|--|
| N-acetylcysteine | 35 of 444 patients (7.8%) |
| Control | 82 of 441 patients (18.6%) |

N-acetylcysteine

Studies of N-acetylcysteine used to prevent contrast-induced nephropathy have produced mixed results. A meta-analysis by Alonso et al¹⁰ attempted to reconcile previous findings but showed large disparities between study designs. The most important disparities were in N-acetylcysteine dosages and hydration protocols used for different patients. Most patients received N-acetylcysteine 600 mg twice daily for two days, starting on the day before the procedure. The authors¹⁰ concluded that N-acetylcysteine reduces the incidence of contrast-induced acute renal failure and may have a greater renal-protective effect in high-risk patients

(Table 2). To prevent one case of contrast-induced acute renal failure, the number needed to be treated with N-acetylcysteine was eight.¹⁰

Bicarbonate Infusion

Use of iso-osmolar crystalloids has been the mainstay of hydration protocols for preventing contrast-induced nephropathy. Merten et al¹¹ recently compared periprocedural use of two substances—sodium bicarbonate and isotonic sodium chloride—and hypothesized that alkalinizing the tubular environment with bicarbonate infusion would reduce formation of free radicals and would decrease the incidence of acute renal failure occurring after exposure to contrast agents.

In that study,¹¹ 119 patients were randomized to receive infusion of either normal saline or sodium bicarbonate before and after administration of the contrast agent. One hour before this administration, patients received either sodium chloride or sodium bicarbonate as a bolus of 3 mL/kg over one hour; infusion of the same substance then continued at a rate of 1 mL/kg/hr for six hours. Interim analysis showed that acute renal failure was developing at a higher rate in the group receiving sodium chloride, and the study was halted. Subsequently, all patients received sodium bicarbonate and were enrolled in a registry so that their progress could be monitored. The results are shown in Table 3. The absolute risk reduction of nephropathy for patients receiving sodium bicarbonate infusion was 11.9%. To prevent one case of contrast-induced acute renal failure, the number needed to treat with sodium bicarbonate infusion was 8.4.¹¹

Conclusion

Acute renal failure sometimes occur after administration of contrast agents. This failure is usually associated with only slight elevation in serum creatinine level and is often self-limited. Treatment of contrast-induced nephropathy focuses on assessing risk factors. Moreover, treatment with N-acetylcysteine as well as hydration with sodium bicarbonate appears to have a renal protective effect in high-risk patients.

Future research will investigate further questions in this field. Researchers have not yet clarified whether a synergistically protective relation exists between N-acetylcysteine and bicarbonate infusion in preventing contrast-induced nephropathy. In addition, researchers will probably examine the effectiveness of prolonged preprocedural bicarbonate infusion and oral bicarbonate supplementation for preventing contrast-induced acute renal failure.

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To conclude the opening case, the patient's creatinine level peaked at 4.9 mg/dL on the fourth day after catheterization. The creatinine level returned to baseline over the next several days while the patient received supportive care only. Although the hospital stay was longer than originally anticipated, dialysis did not become necessary. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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| Table 3. Results of study¹¹ comparing bicarbonate infusion to sodium chloride for preventing contrast-induced acute renal failure | |
|---|---|
| Group | Incidence of acute renal failure |
| Sodium Chloride Infusion Study Group | 8 of 59 patients (13.6%) |
| Bicarbonate Infusion Study Group | 1 of 60 patients (1.7%) |
| Bicarbonate Infusion Registry Group | 3 of 191 patients (1.6%) |

Things Make Sense

Hope is not the conviction that things will turn out well,
but the certainty that things make sense regardless of how they turn out.

— Vaclav Havel, Czech writer, dramatist and former President of Czechoslovakia