Clinical Questions #3

Preventing contrast-induced nephropathy: A basic solution

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Patient
A 54-year-old hypertensive, diabetic male has an abnormal cardiac stress test during workup for exertional dyspnea. He has stage III chronic kidney disease, with an estimated GFR of 40 mL/min. He is admitted for cardiac catheterization.

Clinical Question
In a diabetic patient with chronic kidney disease, does intravenous infusion of sodium bicarbonate prior to cardiac catheterization plus administration of N-acetylcysteine decrease the incidence of contrast-induced nephropathy when compared with infusion of normal saline plus N-acetylcysteine?

How and where could you locate evidence to answer this question?

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How would you treat this patient?

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Turn the page for one possible approach.
Suggested Approach for Clinical Question #3

Search Strategy
1. Cochrane Database of Systematic Reviews (1st Quarter 2005) using OVID interface:
   a. “renal failure or nephropathy or renal insufficiency”
   b. “contrast or dye”
   c. “bicarb$”
   d. combine (a) and (b) and (c)
   e. 4 matches but none applicable to our case
2. Search repeated in Database of Abstracts of Reviews of Effects (DARE) and ACP Journal Club using OVID interface.
   a. 4 matches, none applicable to our case
3. All years of MEDLINE (1966-April Week 4 2005) using OVID interface:
   a. “exp bicarbonate” (exploded MeSH heading)
   b. “exp contrast media” (exploded MeSH heading)
   c. “exp kidney failure” (exploded MeSH heading)
   d. combine (a) and (b) and (c) limited to human studies and English
   e. 1 study that applied to our clinical question: Merten GJ. et al., “Prevention of Contrast-Induced Nephropathy With Sodium Bicarbonate: A Randomized Controlled Trial.”

Study Characteristics
This was a single-center, randomized controlled trial of 119 patients with stable chronic kidney disease (serum creatinine at least 1.1mg/dL) scheduled to undergo a procedure involving the administration of intravenous, radiographic contrast (primarily cardiac catheterization). Patients were randomized to infusion of sodium bicarbonate or infusion of sodium chloride 1 hour prior to and 6 hours following the procedure. The primary endpoint was development of contrast nephropathy, defined as an increase in serum creatinine >25% above baseline within 48 hours of contrast administration.

Validity of Evidence
- Appropriate randomization was performed.
- Follow-up was at least 48 hours, which is probably long enough to evaluate the primary endpoint. However, some authorities allow up to 72 hours for the development of contrast-induced nephropathy.
- There was a 13% dropout rate. This is reasonably complete. However, because the incidence of the primary endpoint was low, even this dropout could introduce bias.
- The analysis was not conducted on an intention to treat basis. Four patients in each group had protocol violations and were excluded from analysis.
- An effort was made to blind patients and clinicians to treatment. Most importantly, laboratory personnel performing the creatinine analysis were blinded.
- Groups were similar at randomization and were treated similarly except for the experimental intervention. Slightly more patients with severe renal insufficiency (Cr >2.5) were randomized to the sodium bicarbonate group than the sodium chloride group. This could bias the results against the sodium bicarbonate group.
- Overall, this study was of good methodologic quality.

Study Results
- 1.7% (1/60) of patients in the sodium bicarbonate group developed contrast-induced nephropathy.
- 13.6% (8/59) of patients in the sodium chloride group developed contrast-induced nephropathy.
- There was an 87.7% (95% CI, 4.7–98.4%) relative risk reduction in the development of contrast-induced nephropathy in the sodium bicarbonate group compared with the sodium chloride group.
- Eight patients (95% CI, 5-38) would have to be treated with sodium bicarbonate to prevent 1 case of contrast-induced nephropathy
- No patients in either group required dialysis. All patients with contrast-induced nephropathy had a prolonged hospitalization.

Applying the Evidence to the Patient
- The patient in the scenario is similar to those in the study. The results can be applied.
- Infusion of sodium bicarbonate is feasible for the patient.

Summary
This is a good quality study that demonstrates a dramatic decrease in the incidence of contrast nephropathy with the use of sodium bicarbonate infusion prior to contrast administration. However, this study does have some shortcomings. The small sample size resulted in relatively wide confidence intervals and made the generally low attrition rate more significant. The data was not analyzed on an intention-to-treat basis, which could lead to an overestimation of the benefits of bicarbonate. None of the patients developing contrast nephropathy went on to require dialysis. The authors note that the length of hospital stay was adversely affected by the development of contrast nephropathy, although they do not report the extent to which this occurred and whether or not the increase in hospital days was significant. This study did not include the use of N-acetylcysteine, which has been shown to decrease the risk of contrast-induced nephropathy in some studies.

Bottom Line
Infusion of sodium bicarbonate dramatically decreases the incidence of contrast nephropathy in patients with chronic kidney disease. Larger studies are needed to further evaluate safety and confirm these results.

Bibliography
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