Bicarbonate and/or Mucomyst vs. Saline alone for Prevention of Contrast-Induced Acute Kidney Injury (CI-AKI)

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Objectives

- Understand role of sodium bicarbonate, sodium chloride, and acetylcysteine in prevention of CI-AKI
- Understand recent literature and guidelines for prevention of CI-AKI
- Be able to apply this information to your current protocol or institution
Overview

- Contrast-induced acute kidney injury (CI-AKI) & contrast induced nephropathy (CIN)
- Defined as a 25% or greater increase in serum creatinine or an increase ≥ 0.5mg/dL with 48 hours
- Accounts for up to 10% of all hospital-acquired renal failure
- Occurs in up to 15% of coronary angiography patients
- Associated with increased morbidity and mortality
  - dialysis
  - Extended hospital stay
  - 1-5 year mortality
May be due to renal vasoconstriction

- Medullary ischemia
- Direct nephrotoxicity & tubular damage
  - Exposure to hyperosmolar contrast media
- DM & CHF
  - Associated with impaired nitric oxide production
    - May lead to increased susceptibility to contrast agents
Risk Factors for Renal Inpairment

- Variety of scoring systems to predict risk of CI-AKI
  - Preexisting renal disease
  - Diabetes mellitus
  - Sepsis or acute hypotension
  - Dehydration
  - Age > 70 years old
  - Cardiovascular disease
  - Previous chemotherapy
  - Organ transplant
  - Nephrotoxic medications
  - HIV/AIDS
  - Highly osmolar contrast has shown to cause direct nephrotoxicity
Sodium bicarbonate:
- Older studies found
  - May decrease risk of CI-AKI
    - Emergency procedures
    - Coronary procedures
    - Patients with CKD

Acetylcysteine:
- In 2000
  - 83 patients, acetylcysteine & 1/2NS vs. placebo & NS
  - Results CI-AKI: Acetylcysteine = 2%, placebo = 21% (p=0.01)
Conflicting conclusions
Publication bias
  - Neutral or negative studies
Heterogeneity
Quality of studies
  - Blinding, incomplete outcome data not addressed
Sodium Bicarbonate

- **Protective Effects**
- **Proposed Mechanism:**
  - Alkalinizing tubular urine may attenuate free radical formation
  - Leading to less oxidant injury & lower rates of contrast induced nephropathy
- **Dose:** 150mEq/L in D5w or SWI
  - One method: bolus of 3ml/kg/hr for 1 hour immediately prior to exposure, then 1ml/kg/IV during and for 6 hours after exposure
Sodium Bicarbonate

- Recent larger studies from 2010:
- Meta-analysis reviewing 18 studies
- Decreased risk of CI-AKI with borderline statistical significance
- No effect on need for dialysis or mortality
- Did not decrease incidence of CI-AKI in 12 of the studies

353 patients with stable renal disease with GFR ≤ 60 mL/min per 1.73 m² & 1 or more risk factors

**Primary Endpoint:** 25% or greater decrease in GFR on days 1-4

**Results:** Sodium bicarbonate = 13.3%, sodium chloride 14.6% (RR = 0.94; 95% CI, 0.55-1.60; P = 0.82)

Rates of death, MI, or CVA did not differ significantly after 30 days or 6 months

- Does not suggest that hydration with sodium bicarbonate is superior to hydration with sodium chloride for prevention of CI-AKI with moderate to severe CKD
Mechanism of Action: -thiol compound with antioxidant & vasodilatory properties
- May minimize vasoconstriction & oxygen free radical generation

Dose: 600mg-1200mg orally BID the day prior and the day of procedure
Acetylcysteine vs. placebo (ACT 2011)

- 2,308 patients undergoing angiography with at least 1 risk factor (age >70, chronic renal failure, diabetes, LVEF<45%, or shock)
- **Primary Endpoint:** CI-AKI 48-96 hours after angiography
- **Results:** Acetylcysteine 12.7%, placebo=12.7% (p=0.97)
- No reduction in CI-AKI with acetylcysteine vs. placebo
Acetylcysteine vs. placebo (LIPSIA-N-ACC, 2010)

- 251 STEMI pts undergoing primary PCI
- Primary Endpoints: Occurrence of CI-AKI & reperfusion injury (myocardial salvage therapy index by MRI)
- Results:
  - CI-AKI: Acetylcysteine=14%, placebo=20% (p=0.2)
  - Reperfusion injury: acetylcysteine =43.5, placebo=51.5 (p=0.36)
- No clinical benefit with acetylcysteine with respect to development of CI-AKI and myocardial salvage index

LIPSIA-N-ACC= Leipzig Immediate Percutaneous Coronary Intervention Acute Myocardial Infarction N-ACC
Practical Concerns

- Drug shortages
- Pharmacy processing
- Patient location
- Taste/palatability
Guidelines & Regimens

- **KDIGO: Kidney Disease Improving Global Outcomes & International Society of Nephrology**
  - IV volume expansion with NS or bicarbonate
    - No clear evidence for an optimal rate or duration, start at least 1 hour before and continue for 3-6 hours after contrast.
  - Recommends oral acetylcysteine w/ IV fluid in high risk patients
    - Does address the lack of consistent data & recommends due to low risk of adverse events and low cost

- **American College of Radiology 2010 guidelines:**
  - Hydration with normal saline and consider acetylcysteine for high risk patients

Contrast-Induced AKI: Recommendations

1. Patients should be assessed for risk of contrast-induced AKI before PCI
2. Patients undergoing cardiac catheterization with contrast media should receive adequate preparatory hydration
3. In patients with CKD (creatinine clearance <60 mL/min), the volume of contrast media should be minimized

CLASS III: NO BENEFIT (Not helpful, no proven benefit)
1. Administration of acetylcysteine is not useful for the prevention of contrast-induced AKI
Review protocols currently in place at your institution

Work with specialty groups (nephrology, cardiology, radiology) to see if changes at your institution can be made to reflect recent literature and guideline updates
References

7. Sodium Bicarbonate vs Sodium Chloride for the Randomized Trial Patients Undergoing Coronary Angiography: A Prevention of Contrast Medium Induced Nephropathy inBrar et al. JAMA. 2008;300(9):1038-1046