10/21/2007

Acetylcysteine to Prevent Angiography-Related Renal Tissue Injury (The APART Trial)

(1)

The American Journal of Cardiology - 2/1/2002
Volume 89 (3) : Pages 356-358

Contrast-Induced Nephropathy:

- contrast agents induce:
  - (A) vasoconstriction-mediated medullary ischemia
  - (B) Direct glomerular cytotoxicity
- then renal reperfusion
  - ↳ release of reactive cytokines / O_2 metabolites ↓ mediate tissue injury

N-Acetylcysteine (NAC):

- scavenges reactive O_2 metabolites
- inhibits synthesis of deletirious proteins / cytokines

Study Design:

- Randomized — n = 54
- Double-blind
- Placebo-controlled

- measured renal function x2 one wk before cath
- f/u renal function @ 24 hrs. +48 hrs. post-cath
- used non-ionic, low-osmol contrait agent (Ioxilan)
- pt's randomized to:
  - (1) NAC 600 mg PO BID x4 doses
  - or
  - (2) Placebo
  - one dose pre-cath and 3 doses post-cath
- All pt's → IV ½ NS @ 1 ml/kg/hr for 2-12 hrs. pre-cath and 12 hrs. post-cath

Inclusion Criteria:

① Stable CRI (creat ≥ 1.4 mg/dL or CrCl < 50 mL/min via Cockcroft-Gault Eq.

② Elective Cardiac cath

Exclusion Criteria:

① Hemodynamic Instability → SBP < 90 or DBP < 50
② Untreated GI Bleeding
③ Known sensitivity to NAC and/or contrast agents
④ Theophylline, Mannitol, Ciprofloxacin or Bactrim tx
⑤ Inability to provide written informed consent

Primary End Point:

Post-cath nephropathy → ↑ creat by ≥ 0.5 mg/dL or > 25 % ↑ in baseline (48 hrs. post-cath)

Outcomes:

① 2/25 (8%) of pt's in NAC group vs. 13/29 (45%) of pt's in placebo group developed primary end point
p = 0.005 RR = 0.21 (95% CI 0.06 to 0.8)

② Mean creat ↓'d from 1.66 (± 0.06) to 1.53 (± 0.09) in NAC group vs. ↑ from 1.56 (± 0.05) to 1.88 (± 0.09) in placebo group @ 48 hrs. post-cath
p < 0.0001 (95% CI −0.6 to −0.3)

③ 6/25 pt's in NAC group had baseline creat ≥ 2 mg/dL and 0/6 of them developed primary end point while 4/29 pt's in placebo group had baseline creat ≥ 2 mg/dL and 3/4 of them developed it p = 0.01

(4) PvD
Renal Artery Stenosis
Contrast Dose > 220 mL
→ Assoc. w/ primary end point
$p < 0.05$

Post-Catheterization Nephropathy			Outcome	No Outcome		Risk of Outcome	Risk of Outcome
(Primary Outcome: p = 0.005)	Treatment (Y)	||	2	23	||	0.08000	=a/(a+b)
	Control (X)	||	13	16	||	0.44828	=c/(c+d)

RR (Relative Risk) or Hazard Ratio: RR = (a/a+b)/(c/c+d)	0.17846	RRR (Relative Risk Reduction): RRR = 1-RR x100 (%)	82.15385%
ARR (Absolute Risk Reduction): ARR = (X Risk - Y Risk) x100 (%)	36.82759%	NNT (Number Needed to Treat): NNT = 1/ARR	3

==========

Post-Cath Nephropathy & Baseline Creat ≥ 2mg/dL			Outcome	No Outcome		Risk of Outcome	Risk of Outcome
(Secondary Outcome: p = 0.01)	Treatment (Y)	||	0	6	||	0.00000	=a/(a+b)
	Control (X)	||	3	1	||	0.75000	=c/(c+d)

RR (Relative Risk) or Hazard Ratio: RR = (a/a+b)/(c/c+d)	0.00000	RRR (Relative Risk Reduction): RRR = 1-RR x100 (%)	100.00000%
ARR (Absolute Risk Reduction): ARR = (X Risk - Y Risk) x100 (%)	75.00000%	NNT (Number Needed to Treat): NNT = 1/ARR	1