Contrast Nephropathy – Too Much or Too Little Concern?

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Disclosures

• Fresenius Medical Advisory Board

• Research / Grants
  • C.R. Bard
  • Humacyte
  • Vascular Therapies, Inc.
  • W L Gore

• None of this pertinent to this presentation
Please note

WE WILL NOT BE DISCUSSING GADOLINIUM OR NEPHROGENIC SYSTEMIC FIBROSIS, JUST IODINATED CONTRAST
Contrast Nephropathy – What is it?

• Acute Kidney Injury occurring after exposure to iodinated radiocontrast media*

• Usually reversible (but not always) **


Contrast Nephropathy – Possible Etiology

- Actual cause not well understood
  - Tubular hypoxia and injury*
  - Viscosity**
  - Vasoconstriction due to endothelial factors***
  - Direct toxicity to tubular cells****

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Tubular Hypoxia and Injury

- Inhibit mitochondria activity*
  - Increase adenosine by hydrolysis of ATP
  - Adenosine + Medullary Hypoxia generates “Oxygen Radicals”
  - These radicals “scavenge” Nitric Oxide

Tubular Hypoxia and Injury

- Increased oxygen consumption via Endothelin-A receptor*, **
- Possible direct cytotoxicity d/t altered integrity of membranes***

Viscosity / Osmolality

• Other substances like Mannitol or Hypertonic Saline cause similar histology*

• Contrast enters tubule and, especially with any volume depletion, becomes more concentrated affecting tubular flow / fxn**

• Increased blood viscosity affecting red cell deformability and increasing resistance to blood flow***

Vasoconstriction – Direct and Indirect

• Direct release endothelin and prostaglandins*
  • With adenosine activates A1 receptor constricting afferent arteriole
  • But also medullary vasodilatation vs constriction due to multiple mediators

• Direct action of contrast on vascular smooth muscle cells**

• Makes any pre-existing vascular pathology worse***

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***Lameier NG. Nephrol Dial Transplant. 21(6):i11-23, 2006
Direct Tubular Toxicity

• Direct effect of contrast on tubular cells*, **
• Cytotoxicity causes apoptosis of tubular cells***
  • Cellular casts obstruct

Radiocontrast Nephrotoxicity – Major Risks

- Decreased GFR
- Proteinuria
- Age
- Presence of DM
- Dose of Contrast
- Type of Contrast

- ACEI / ARB Use
- Volume Status
- PG Inhibition
- Hyperviscosity Syndromes
Radiocontrast Nephrotoxicity – Major Risks

• Decreased GFR
  • In absence of CKD, risk $\leq 1\%$ *
  • For those with decreased renal function, incidence after contrast study is 10 to 30% **
  • Incidence of Contrast AKI increases proportional to baseline decrease GFR***

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Radiocontrast Nephrotoxicity – Major Risks

- Proteinuria
  - Additional risk factor for contrast nephropathy*
  - May be an independent risk **

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Radiocontrast Nephrotoxicity – Major Risks

• Age
  • GFR tends to decrease with aging even in normal
  • Association between age ≥ 65 and AKI from contrast*
  • Age > 75 associated with 1.5 to 5x increased risk with increased incremental risk with each additional year of age**
  • BUT another retrospective review of 5006 patients did not find age to be a risk factor***

• Perhaps age, by itself is not the issue but co-morbidity is

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Radiocontrast Nephrotoxicity – Major Risks

• Presence of DM
  • Increased oxygen consumption in DM kidney*
  • Increased snGFR in diabetic kidney**
  • Often see micro and macro vascular disease in DM***

• Diabetic status associated with bloodflow issue, increased snGFR, hampered antioxidant capacity, altered sensitivity to chemical mediators ****

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Radiocontrast Nephrotoxicity – Major Risks

• Dose of Contrast
  • More contrast amount leads to more AKI*
  • Safety demonstrated with <10mL fistula study in CKD population**
  • Safety demonstrated with IV vein mapping in CKD (<20 mL contrast)***

Radiocontrast Nephrotoxicity – Major Risks

• Type of contrast*
  • New lower osmolar agents possibly less risk BUT data not conclusive*
  • Iodixanol may have a unique benefit over others BUT AGAIN, conflicting data and studies exist**

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Radiocontrast Nephrotoxicity – Major Risks

- ACEI / ARB Use
  - May be an independent risk factor for contrast AKI*
  - Significant increase (11.4 vs 6.3%) in patients on ACEI/ARB**
  - BUT, other data suggests no association***

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Radiocontrast Nephrotoxicity – Major Risks

• Volume Status
  • May be relative issue (decreased cardiac, etc)
  • Can adversely affect GFR increasing risk
  • Can lead to more avid re-absorption and even higher osmotic forces in tubules
  • Some conflicting data but most accept as a risk factor*

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Radiocontrast Nephrotoxicity – Major Risks

• **PG Inhibition**
  • NSAIDs can adversely affect renal function especially with dehydration or decreased effective renal bloodflow*
  • Any decrease GFR can increase risk of contrast nephropathy
  • Prostaglandins involved in response to contrast**
  • Not clear that NSAIDs increase risk of contrast nephropathy independently**

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Radiocontrast Nephrotoxicity – Major Risks

- Hyperviscosity Syndromes
  - Can cause pre-existing issues with microscopic bloodflow
  - Incidence 0.6 – 1.25% in MM patients compared to normal*
  - Subsequent review showed little correlation in MM patients with normal GFR but correlation to b2-macroglobulin levels**

- Risk may be due to the effect of the disease and not the viscosity

*McCarthy CS and Becker JA. Radiology 183(2):519-521, 1992
Contrast Toxicity – Is it so bad?

• Acute
  • Transient decrease renal function 3 to 7 days after exposure
  • Most recover after 5 to 7 days from peak
  • Some may have persisting decrease GFR compared to baseline
  • Length of stay and short term mortality higher*
  • More likely to require renal replacement therapy**

Contrast Toxicity – Is it so bad?

• Long term
  • Risk of cardiovascular, cerebrovascular, and all cause mortality increased*
  • Worse “event-free” outcomes in those with contrast nephropathy**
  • Even in those that recover, long term mortality increased

• But, effect of nephropathy or of co-morbidities?

Contrast Toxicity – Is it so bad?

• The water is muddy*
  • Contrast?
  • Atheroembolic disease?
  • Co-morbidities?
  • “Selection bias?”

• Which patients get these studies?

Contrast Toxicity – Can we prevent?*

- Mannitol / Lasix
- Ca++ Blockers
- Dopamine / Fenoldopam
- Endothelin Receptor Antagonist (Ambrisentan)
- Prostacycline
- Atrial Natriuretic Peptide
- Adenosine Agonists (Theophylline, Aminophylline)
- Bicarbonate
- Statins
- Acetylcysteine
- Fluids
- Limit exposure

N-Acetylcysteine?

“The only well established treatment for the prevention of CIN is intravenous hydration”

Steven Fishbane

CJASN 3(1):281-287, 2008

Contrast Toxicity - Treatment

• Avoid further insult
• Fluids
• Bicarb?
• Diuretic?
• Dialysis
Contrast Nephrotoxicity - Perspective

• Avoid – No Contrast, No Toxicity
  • Find alternate diagnostic study

• Use less
  • Angiography in CKD
  • Vein mapping in CKD
Contrast Nephrotoxicity - Perspective

- Avoid
- Use less
- Hydrate
- Bicarb?
Contrast Nephrotoxicity - Perspective

- Avoid
  - Find alternate diagnostic study
  - Use less
- Hydrate
- Bicarb?
- Acetylcysteine?
Contrast Nephrotoxicity - Perspective

• Avoid
  • Find alternate diagnostic study
  • Use less

• Hydrate
  • Low ionic dye
  • Bicarb?
  • Acetylcysteine?

• Be afraid! (Dry, DM, GFR, Hyperviscosity, NSAIDs)
Contrast Nephrotoxicity - Perspective