The Weekly Probe

8th November 2016 **Volume 19 Issue 37**

Paediatric Dosing- please be careful with drug dosing in kids. Check weights. Use one of the paediatric pharmacopaedias such as the Australian Medicines Handbook Childrens' Dosing Companion or MIM via CIAP and record the weight based calculation on the medication chart. Also check your decimal points with a colleague if unsure. Please be careful!

Phenytoin toxicity- A warning from the UK regarding a cardiac arrest in a child after being given phenytoin. It has antiarrhythmic properties so 15–20 mg/kg by slow injection or IV infusion (1–2 mg/kg/minute, not to exceed 50 mg/minute). If toxicity is encountered, the management is largely supportive yet the warning says intralipid may be used – speak to Poisons on 131126 ASAP.

THIS WEEK

LAST WEEK'S CASE- CONTRAST NEPHROPATHY

A 65yo lady with diabetes and eGFR 35ml/min presents with abdominal pain. Ischaemic gut is one diagnostic possibility and you are considering a CT with contrast yet you are concerned about contrast nephropathy. What can we do to minimise these risks?

Definition

- Acute renal impairment following IV contrast in the absence of other causes
- An increase in serum creatinine >44 umol/l
  OR
  a 25% or greater relative increase from baseline 48–72 h after administration of contrast.
- Terms include contrast nephropathy contrast-induced, acute kidney injury (AKI), contrast induced nephropathy (CIN)

Pathogenesis - Multiple aetiologies. Contrast results in transient vasodilation followed by arteriolar vasoconstriction resulting ischaemia to the renal medulla. Water soluble contrast is also filtered and when taken up by the tubular cells results in cellular swelling, loss of function and cellular death. This results in further tubular and parenchymal injury.
Statins may have beneficial effects at the level of this tubular injury while alkalinisation may reduce the precipitation of protein in the tubules.
The natural history of CIN follows a time course of 8-10 days with repair and regeneration yet with repeated contrast doses and pre-existing renal problems there may be delayed or no recovery.
It's important to note that subclinical CIN may occur to different extent in every patient exposed to iodinated contrast.

Who gets it ? - Risk Factors

- Renal Insufficiency - Cut Off Creat >132 umol/l or eGFR <60
- Extra Caution in Renal Impairment
  + Diabetes
  + Reduced renal perfusion (eg. Cardiac Failure, shock)
- Amount of contrast given (PCI (150-200ml- c/w most CTs 30-50ml), repeated CT scans)
-

Patient-related factors	Procedure-related factors
Underlying renal insufficiency	Volume of contrast used
Diabetes mellitus*	Hyper-osmolal contrast media
Intravascular volume depletion	Intra-arterial contrast administration
Congestive heart failure	

- *Amplifies risk in the setting of renal insufficiency.

Using these factors scoring systems have been developed to predict a post–percutaneous coronary intervention range of CI-AKI from a rate of 7% for those at lowest risk to a rate of >50% for those with the highest risk score.

Clinical Characteristics

- Begins 12- 24hrs after contrast administered
- In vast majority is nonoliguric - mild and transient - recovery begins in 3-5 days reversible and normalises by day 14. Some call it a creatininopathy as compared to a cretinopathy, endemic to some pockets of this area health service.
- Things to exclude:
  - Acute tubular necrosis
  - Acute Interstitial nephritis
  - Atheroemboli (especially in PCI).

Things To Do

- Avoid when possible
  - Do they really need the scan?
    Ultrasound or CT with no contrast an option?
    VQ scan instead of CTPA
    MRI if CT brain angiography needed

- Optimise condition prior to Scan
  - Delay till condition improved
  - Cease nephrotoxins – NSAIDs , Gentamicin- cease ACE-I/ARB (increased Odds Ratio by 6 X if not ceased 48 hrs pre-contrast)
  - Correct dehydration
  - Avoid repeated or closely spaced scans < 48 hrs apart - lower doses of contrast

Pre-Hydration - Most guideline emphasise pre-Hydration - Most animal studies convincingly show that being volume deplete is harmful

- How ? Oral vrs IV - Unrestricted oral fluid did worse than those given iv saline. 34.6%vs 3.7%
- (Although salt loading has the same efficacy as iv saline (1g/10kg/day)- never trialled to see if putting this on a $5 bag of chips makes any difference in outcome

  What ? Isotonic Saline (0.9% NaCl) have shown an improvement when compared to ½ Isotonic Saline (0.45% NaCl) - 0.7% vs 2.0% $p<0.04$

Bicarbonate – there was a thought that volume load + improves urinary alkalinisation with antioxidant properties on tubules may reduce the risk of CIN . Isotonic bicarbonate is prepared by mixing 850ml 5% dextrose with 150ml (3 ampoules) of 8.4% bicarb. The article “Strategies for the prevention of contrast-induced acute kidney injury” in Current Opinion in Nephrology and Hypertension Volume 19(6), November 2010, p 539–549 concludes..

> “At this time, data on the comparative effectiveness of bicarbonate and saline for the prevention of CIAKI are insufficient to warrant a recommendation for the routine use of a specific isotonic i.v”.

Likewise the International society of Nephrology recommends an isotonic solution of either normal saline or bicarbonate as although there is “a possible but inconsistent benefit of bicarbonate solutions based on overall moderate-quality evidence” there may be issues with the extra burden of drawing up the bicarb and the dosing errors (!!) ie best to keep it simple

A suggested regimen of crystalloid hydration is :

- 3 mL/kg of normal saline for one hour prior to the procedure, and continued at a rate of 1 -1.5 mL/kg per hour for 4-6 hours after the procedure- longer if dry or more impaired renal function.
- For inpatients this may be continued for 12-24 hrs

Others -

- Forced Diuresis does not work- In fact more harmful
  -11% AKI with fluids / 28% with mannitol / 40% with furosemide

Editor: Peter Wyllie

- Dopamine - No improvement
- Inhibitors of Vasoconstriction- Some agents prevent vasoconstriction eg. calcium channel blockers (theophylline, aminophylline, nifedipine, captopril, prostaglandin, low dose dopamine) - Not really found to be beneficial in studies and most were underpowered.
- Theophylline – High quality studies showed no difference while metanalysis may show lower creatinine peaks yet but not rates of developing CIN. No difference in need to dialyse and mortality.
- Ascorbic Acid - no evidence of benefit

- Statin (High or low dose) – jury awaiting further trials – insufficient evidence to support routine use - One metanalysis of 8 trials (4734 patients) found that CIN occurred in 3.3% treated with statins versus 6.4% of the placebo group [OR 95% CI 0.50 (0.38-0.66), p < 0.00001) – including both short term high dose and long term low dose statins.
    - The PRATO-ACS study used rosuvastatin 40mg then 20mg daily for statin naïve patients undergoing PCI –found AKI in 6.7% vrs 15.1% OR 0.38
    - Another study by Han used rosuvastatin 10mg 2 days pre continued for 5 days with a reduction of AKI from 3.9% to 2.3% ie 41% reduction

Prophylactic Dialysis Pre-contrast- No benefit- Harmful especially in more severe CRF

- Hydration + NAC– C.I.N 4.3% OR 0.5
  Hydration alone 7.2% OR 1
  Hydration + Dialysis 16.4% OR 2.5

Dialysis post-contrast?
- Retrospective analysis of 58,000 patients < 0.1% (n=59) required dialysis
- General incidence 0.4%-0.8%
- Patients who require dialysis are those who were going to end up on dialysis either way

N-Acetylcysteine- controversial as there is conflicting data. At times an inpatient team requests certain interventions yet remember that if used, it should be started 24 hours before the procedure and continued for 24 to 48 hours after exposure to contrast, at a dose of 600 -1200 mg orally or intravenously every 12 hours. There is, however, no evidence that N-acetylcysteine alters mortality or renal outcomes if given perioperatively when radiocontrast is not used.
- **Oral** - Inexpensive with no toxicity but stinks (ie malodorous). Oral route is preferred option in most guidelines. Note that we only stock a IV 20% preparation which can also be used for nebulisation. American sites suggest diluting the 20% solution up as an oral preparation to 5% yet the Australian Medical handbook or MIMs does not cover the use of NAC in prevention of contrast nephropathy or the oral use of NAC.
    - In PCI studies – CIN in 5% given 1600mgBD, 15% usual dose, 30% placebo.

- **IV NAC** - Administration also comes with a reasonable risk of anaphylactoid reaction (14.6% in one trial).

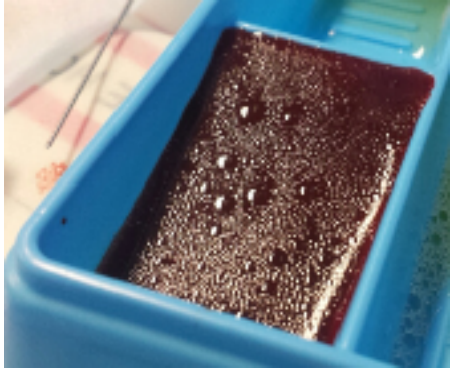
Take Home Points
- Stratify risk of complications (CIN)
- Don't do the scan with IV contrast if alternative possible (or delay till improved)
- Avoid repeated scans
- Stop toxins – NSAID, ACE/ARB
    - ACE =the "..prils" (eg Lisinopril, enalapril) - ARBs = the "..tans" (eg irbesartan, candesartan)
- Prehydrate (and post-hydrate) with isotonic solution IV (saline or bicarb)
- Consider a statin- considering the huge number of people in the community who take these for questionable reasons over prolonged periods, this is one intervention that has little downside and may make a difference when you are worried about CIN.
- Can give oral NAC 600mg or 1200 mg BD 2 days pre and post scan

Additional Refs – McCullough PA et al, Contrast-Induced Acute Kidney Injury J Am Coll Card 2016; 8(13) / Best Bets / Up-to-date / BMJ Best Practice http://www.kdigo.org/clinical_practice_guidelines/pdf/KDIGO%20AKI%20Guideline.pdf
http://emedicine.medscape.com/article/246751-treatment#d13

NEXT WEEK'S CASE

A 65yo man presents with knee swelling post trauma and the Xray shows an effusion only. The knee is aspirated. Below is the aspirated blood. What does it show and what does this indicate?

Editor: Peter Wyllie



JOKE / QUOTE OF THE WEEK

"Say what you will about Trump, he is not stupid. He is a smart man with a deep understanding of what stupid people want."—Andy Borowitz

Sorry - 2 dad jokes :

- " I used to go out with an archeologist but I hate to dig up the past"
- "I keep falling off my bike- It's just a vicious cycle"
-

Please forward any funny and litigious quotes you may hear on the floor (happy to publish names if you want)

THE WEEK AHEAD

Tuesdays - 14:30 – 15:30 Intern & JMO teaching -Thomas & Rachel Moore
Wednesday- 0800-0900 Critical Care Journal Club. ICU Conf Room / 14:30 – 15:30 Intern & JMO teaching -Thomas & Rachel Moore
Thursday 0730-0800 Trauma Audit. Education Centre / 0800-0830 MET Review Education centre / 1300-1400 Medical Grand Rounds. Auditorium.

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