### Imaging with iodine based contrast agents in adults - Guideline for the prevention of contrast induced nephropathy

<table>
<thead>
<tr>
<th>Document Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Version:</strong></td>
</tr>
<tr>
<td><strong>Date:</strong></td>
</tr>
<tr>
<td><strong>Authors (incl. job title):</strong></td>
</tr>
<tr>
<td>Dr. C. Jason Wilkins (Consultant Radiologist)</td>
</tr>
<tr>
<td>Dr. P. Kane (Consultant Radiologist)</td>
</tr>
<tr>
<td>Dr. J. Wendon, (Consultant Intensivist)</td>
</tr>
<tr>
<td>Dr. P. Donohoe, (Consultant Nephrologist)</td>
</tr>
<tr>
<td>M. O. Chai, (Senior Pharmacist Renal Services)</td>
</tr>
<tr>
<td><strong>Responsible committee or Director:</strong></td>
</tr>
<tr>
<td><strong>Review date:</strong></td>
</tr>
<tr>
<td><strong>Target audience:</strong></td>
</tr>
<tr>
<td><strong>Stakeholders/committees involved in guideline development:</strong></td>
</tr>
</tbody>
</table>

---

For Evidence Based Practice Committee’ use only

| **Ratified by:** | Evidence Based Practice Committee |
| **Date ratified:** | |
| **Reference No.:** | 3805 |
| **Date when guideline comes into effect:** | |
| **Conforms to Group format:** | |
Imaging with iodine based contrast agents in adults - Guideline for the prevention of contrast induced nephropathy

BACKGROUND

Intravascular iodine based contrast is widely used in diagnostic imaging such as CT scanning, intravenous urography (IVUs), and peripheral and coronary angiography. Its use is associated with significant morbidity due to contrast-induced nephropathy (CIN). CIN is a common cause of acute renal failure (ARF) in hospitalised patients. CIN is defined as an acute deterioration in renal function, with a rise in serum creatinine of >25% of baseline value occurring 24 to 48 hours after intravascular injection of iodinated contrast media and without alternative explanation. This guideline is written following a local response to the Royal College of Radiology paper, 'Standards for iodinated intravascular contrast agent administration to adult patients'. The aim is to provide guidance on preventative measures for CIN following administration of iodinated intravascular contrast agent in at risk patients.

RISKS FOR CONTRAST INDUCED NEPHROPATHY

At risk patients:

Chronic kidney disease is the single most important predictor of CIN, where it is associated with 20 fold increase in developing CIN. Patients should be assessed for the presence of factors predictive of possible pre-existing chronic kidney disease or risk of acute renal failure, particularly sepsis and hypotension (table 1 below describes some of the predisposing risk factors for acute or chronic renal impairment and/or development of CIN). Risk of CIN should be assessed using eGFR and not absolute serum creatinine (table 2 below summarises the risk of CIN based on eGFR). Extra care should be taken in patients in whom eGFR is inaccurate eg liver failure and clinical judgement exercised.
Table 1: Risk factors for acute or chronic renal impairment and/or development of RIN

<table>
<thead>
<tr>
<th>Non-modifiable</th>
<th>Modifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Renal disease or solitary kidney</td>
<td>- Concomitant use of nephrotoxic</td>
</tr>
<tr>
<td>- Diabetic nephropathy</td>
<td>- drugs and/or renal perfusion</td>
</tr>
<tr>
<td>- Age &gt; 70 years</td>
<td>- reducing agents *(i.e. ACEIs)</td>
</tr>
<tr>
<td>- Previous chemotherapy</td>
<td>- NSAIDS, aminoglycosides,</td>
</tr>
<tr>
<td>- Organ transplant</td>
<td>- vancomycin, diuretics) *check</td>
</tr>
<tr>
<td>- Cardiovascular disease</td>
<td>- with pharmacist if unsure</td>
</tr>
<tr>
<td>- Patients recovering from acute renal failure due</td>
<td>- Dehydration / volume contraction</td>
</tr>
<tr>
<td>to acute tubular necrosis (ATN) are at particular</td>
<td>- Hypotension (Systolic blood pressure &lt; 80mmHg)</td>
</tr>
<tr>
<td>risk</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Risk assessment is based on eGFR rather than the absolute level of serum creatinine

<table>
<thead>
<tr>
<th>eGFR</th>
<th>Description of renal function</th>
<th>Risk of CIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 45ml/min</td>
<td>Normal or near normal renal function</td>
<td>Low</td>
</tr>
<tr>
<td>30-45ml/min</td>
<td>Moderate renal dysfunction</td>
<td>Low to moderate</td>
</tr>
<tr>
<td>&lt; 30ml/min</td>
<td>Severe renal dysfunction (i.e. AKI)</td>
<td>High risk</td>
</tr>
<tr>
<td>&lt; 10ml/min</td>
<td>Already established on Renal Replacement therapy – not at risk unless recovery phase of ATN/AKI</td>
<td>Fluid balance may be an issue with large volumes of contrast</td>
</tr>
</tbody>
</table>
STRATEGIES FOR PREVENTION OF CIN

1. CESSATION OF NEPHROTOXIC DRUGS WHERE SAFE TO DO SO
2. OPTIMISATION OF HYDRATION STATUS
3. N-ACETYLCYSTEINE (NAC) ADMINISTRATION PRIOR TO IODINATED CONTRAST
4. CHOICE OF CONTRAST AGENT
5. CONSIDER ALTERNATIVE INVESTIGATION IF AT RISK OF CIN

In High Risk patients iodinated intravascular iodinated contrast agents should only be administered following pre-hydration and NAC prophylaxis with consideration of the above guidelines (see below for suggested regimens).

At Risk patients include:

1. all those in the High Risk group (eGFR <30 ml/min) and
2. those with low to moderate risk based on eGFR alone (eGFR 30-45 ml/min) with additional risk factors e.g. ATN recovery phase, diabetes, renal transplant –clinically consider treating as belonging to the High Risk Group.

1) CESSATION OF NEPHROTOXIC DRUGS WHERE SAFE TO DO SO

Nephrotoxic drugs should be discontinued at least 48 hours prior to the procedure.

- Non-Steroidal Anti-inflammatory Drugs (NSAIDs) - e.g. ibuprofen, diclofenac
- Diuretics - e.g. metolazone, bendrolothiazide, furosemide
- ACE inhibitors - e.g. ramipril, enalapril, lisinopril, perindopril
- Angiotensinogen Receptor Blockers (ARB) - e.g. irbesartan, losartan, candesartan
- Metformin (should be stopped on the day of contrast administration and not re-started for at least 48 hours and only if renal function remains stable after receiving iodinated contrast)

Check with your pharmacist if you are unsure.
2) OPTIMISATION OF HYDRATION STATUS
Prescribe one of the following pre-hydration regimens on patient’s fluid prescription once a procedure requiring iodinated contrast is identified. This will enable nursing staff to administer the fluids as soon as the time of the procedure is known.

SUGGESTED FLUID REGIMENS

A. In-patient intravenous regimen

1. No significant cardiac history / contra-indication to fluid loading
Administer 0.9% sodium chloride IV infusion or Hartmann’s solution at rate of 1ml/kg/hr (maximum of 100ml/hr) 6 to 12 hours prior to the procedure and continue for 6 to 12 hours post contrast administration.

2. Patient with congestive heart failure or left ventricular ejection fraction <40%
Administer Sodium chloride 0.9% infusion or Hartmann’s solution at rate of 0.5ml/kg/hr (maximum 50ml/hr) 12 hours pre- and 12 hours post-procedure

3. Alternative regimen: isotonic sodium bicarbonate 1.26% together with intravenous NAC in high risk patients:
   1. Isotonic sodium bicarbonate (1.26%) may be used in combination with NAC, particularly in these high risk patients requiring > 140 ml of contrast media. It is infused at a rate of 3 ml/kg/hour for 1 hour immediately prior to contrast administration, followed by 1 ml/kg/hour during the procedure and for the subsequent 6 hours, as described(2).

B. Outpatient oral hydration regimen

In At Risk out-patients adequate oral hydration is likely to confer some benefit and may be performed on an outpatient basis. 3L/day starting 24 hours pre procedure is recommended unless there are contraindications to fluid loading. This will avoid admission for IV fluids. Oral NAC prophylaxis must also be prescribed as detailed below. **If there are multiple risk factors admission for IV fluids should be considered. This is a clinical decision to be made by the caring physician or surgeon.**
3) N-ACETYLCYSTEINE (NAC) ADMINISTRATION PRIOR TO IODINATED CONTRAST

NAC DOSAGE GUIDELINE FOR ORAL OR INTRAVENOUS ADMINISTRATION

**Oral regimen for At Risk patients:**

*High risk group (<30 ml/min) and Moderate risk group (30-45 ml/min) with additional risk factors.*

NAC 600mg twice daily (PO) pre and post-procedure, up to 48 hours post procedure (6 doses in total, ideally with the first dose given 12 hours pre-procedure).

Advise patient to take the first dose of oral NAC (600mg) 12 hours before the procedure (i.e. the day before the procedure) and the morning before the procedure. Continue oral NAC twice daily for up to 2 days post procedure (i.e. total of 6 doses). Patient should also be advised to maintain oral fluid intake prior to and up to 72 hours after the procedure.

**OR for very high risk patients: multiple risk factors / very low eGFR consider use of high dose oral or intravenous NAC:-**

**HIGH dose oral NAC and Intravenous hydration regimen as above.**

Oral NAC 1200mg twice daily with the first dose 12 hours before the procedure and continue for up to 2 days after the procedure (total of 6 doses).

**Intravenous NAC if Oral NAC not feasible or in Very High Risk Patients**

For Very **High Risk Patients** (eGFR <30 ml/min plus additional risk factors) or where a large volume (>140ml) of iodinated contrast is likely) or if oral NAC administration is not feasible, then consider intravenous NAC pre- and post- procedure as this may confer benefit over oral NAC alone:
**IV NAC infusion** (this regime may not be suitable for patient with CHF – please discuss option with relevant specialist clinical lead)

**2 hours Pre-procedure:**

100mg/kg of IV NAC in 1000ml of Sodium Chloride 0.9% at 150ml/hr

**Post procedure:**

100mg/kg of IV NAC in 1000ml Sodium Chloride 0.9% at 150ml/hr for 4 hours

---

### Contraindications to NAC

**NAC should not be given in the following circumstances:**

- Diagnostic imaging procedure using <30 ml of **intravascular** iodinated contrast
- CKD stage 5 on **long** term renal replacement therapy
- A true allergy response to N-acetylcysteine - common but rarely serious
- Previous anaphylactoid reactions (these occur in around 3% of cases and include angioedema, bronchospasm, urticarial rash and hypotension).
- Patient with an allergy to lactose should avoid oral NAC.

---

### 4) CHOICE OF CONTRAST AGENT

Iso-osmolar contrast agents such as Iodixanol (Visipaque™) should be used where possible in at risk patients especially when this group of patients undergo procedures that need high volume of iodinated contrast agent. It is strongly recommended to give the lowest practical dose suitable for diagnostic purposes. The radiology department will determine the appropriate contrast agent at the time of procedure based on the clinical information available.
Appendix – NAC background

NAC is a thiol-containing antioxidant that has generally been used in acute paracetamol poisoning. Evidence also indicates it may prevent ischaemic-reperfusion syndrome in the heart, lungs, liver and kidneys. There are a number of mechanisms proposed;

1. NAC may scavenge circulating free radicals thereby reducing their ability to directly damage tissues and cells.

2. NAC may chemically bind with nitric oxide to form S-nitrothiyl, a potent vasodilator that increases perfusion to medulla.

3. NAC increases the expression of nitric oxide synthase, which may contribute to enhance renal perfusion.

4. Supporting information in the use of isotonic sodium bicarbonate:
   Free radical formation is promoted by an acidic environment typical of tubular urine but is inhibited by the higher pH of normal extracellular fluid. It has been hypothesized that alkalinising renal tubular fluid with bicarbonate may reduce injury. At physiological concentrations, bicarbonate scavenges peroxynitrite and other reactive species generated from nitric oxide. Postulated that the higher amount of HCO3 in the proximal convoluted tubule may buffer the higher amount of H as a result of cellular hypoxia and facilitate Na reabsorption through the electrogenic Na/HCO3 cotransporter.
References:


5. Standards for iodinated intravascular contrast agent administration to adult patient Royal College of Radiologists. November 2005


