Contrast-induced nephropathy

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Abstract

The use of coronary angiography as a diagnostic tool in modern hospital medicine continues to rise. With the increasing use of therapeutic coronary interventions, and the increases in procedure times and volumes of contrast media, incidence rates of contrast-induced nephropathy (CIN) have also been seen to climb over recent years. CIN has subsequently been shown to be a significant contributor to morbidity and mortality during hospitalisation. In this current clinical setting, it is incumbent on the modern cardiologist to be aware of this potentially serious complication of angiography, to be familiar with its presentation and treatment, and to be able to recognise at-risk groups and institute prophylactic measures where appropriate.

Key words: contrast-induced nephropathy, serum creatinine, hydration, N-acetylcysteine, coronary angiography, contrast media, nephrotoxicity, acute renal failure.

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Introduction

Contrast-induced nephropathy (CIN) is the third most common cause of hospital-acquired acute renal failure, accounting for 10% of cases.[1] In an era of increasing rates of diagnostic and therapeutic coronary interventions, its role in determining outcome of patients undergoing coronary angiography (a population at high risk due to their high incidence of multiple predisposing and complicating risk factors) cannot be overestimated.

Although the decline in renal function is mild and transient in the vast majority of patients who develop CIN, the condition remains a significant source of morbidity and mortality. If a patient is otherwise well, prognosis is generally excellent but mortality is very high in patients with concomitant, persistent multi-system involvement such as circulatory instability, abdominal infection or pneumonia.

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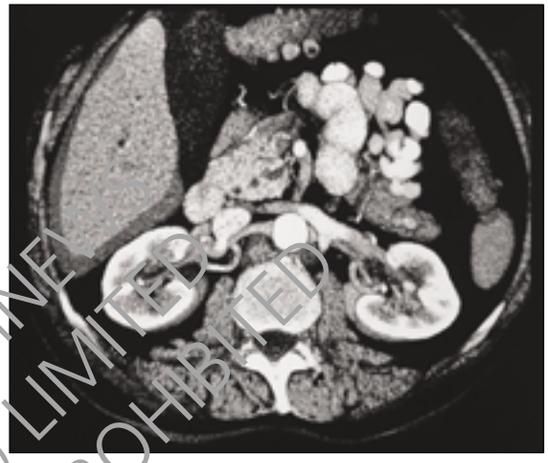
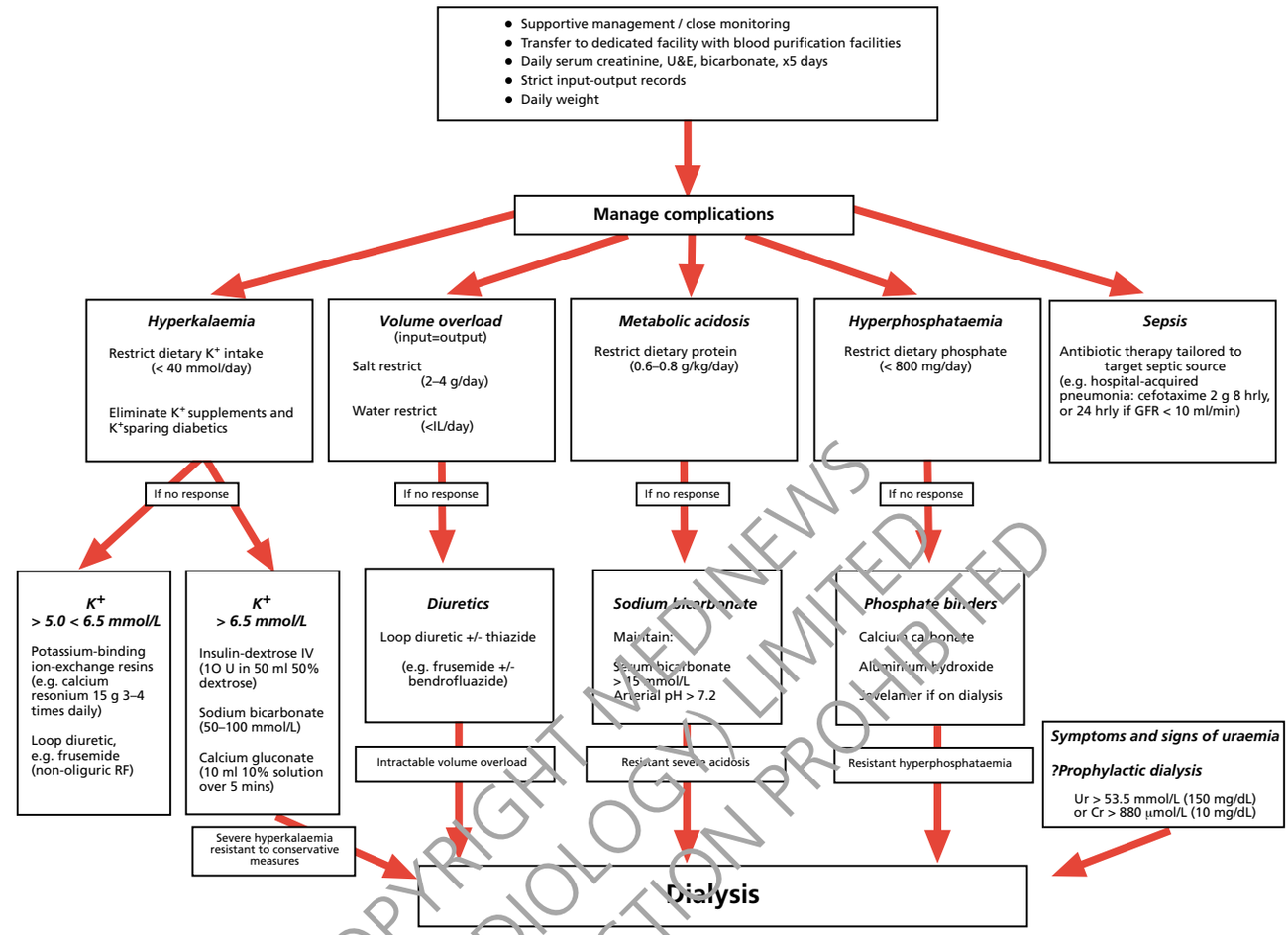
Figure 1. Axial three-dimensional surface-rendered CT reconstruction at the level of the renal arteries



In a large study of coronary angiography patients, of the < 1% of patients who developed acute renal failure requiring dialysis (defined as a decrease in renal function necessitating acute haemodialysis, ultrafiltration or peritoneal dialysis in the first five days post-intervention), mortality rates were found to be over 35%, with two-year survival rates of 18.8%.[2] This reflects previously published overall mortality rates for acute tubular necrosis of 40–60%.[3] Similar findings were reported in another study of over 16,000 patients, which also found that the development of renal failure post-intravenous contrast (defined as an increase in serum creatinine levels of at least 25% from baseline to at least 2 mg/dL) conferred excess risk of mortality, independent of other risk factors. Although only 174 (1%) patients developed acute renal failure in the series, it was found that mortality rates were significantly higher in this cohort when compared with a patient group from the same population who underwent similar contrast-enhanced procedures and were matched for age and baseline serum creatinine, but who did not develop renal failure (34% *vs.* 7%). Levy *et al*. also found CIN to be associated with the development of significant non-renal morbidity such as sepsis, coma, respiratory failure and bleeding. It was also shown that renal dysfunction itself contributed to an

Figure 2. Proposed treatment algorithm of contrast-induced renal failure



Key: U&E = urea and electrolytes; K^+ = potassium; GFR = glomerular filtration rate; RF = renal failure; IV = intravenous; U = units

increase risk of death from pre-existing non-renal conditions, 40–50% of which were accounted for by cardiovascular events.[4]

Definition

CIN is most commonly defined as: 'a 25% increase in serum creatinine concentration from the baseline value, or an absolute increase of at least 44.2 µmol/L (0.5 mg/dL), which appears within 48 hours after the administration of radiocontrast, and is maintained for two to five days'.[5] These arbitrary values were chosen because higher levels of cut-off were found to be less sensitive at predicting incidence of contrast-related renal dysfunction.[6] In addition, a large cohort study found that even apparently small decreases in renal function can lead to excess mortality, independent of other risk factors.[4]

Incidence

Reported incidences of CIN have varied due to inconsistencies in definition of the condition, as well as discrepancies in other areas such as the procedure studied, the type and dose of contrast used, and differences in patient populations. Rates in the general population are estimated as being less than 2%,[7] but incidences between 40% and 90% have been quoted, depending on the number of risk factors present (most notably chronic renal insufficiency, diabetes mellitus with renal impairment, and high volume of contrast administered).[1,5] A more recent large epidemiological study quoted an overall rate of incidence of 14.5%.[2]

Clinical presentation

Although normal renal function can be demonstrated by a number of imaging techniques (see figure 1), no imaging modality has been shown to be consistent in demonstrating CIN. Its detection relies on close monitoring of biochemical profiles. CIN most commonly manifests as an asymptomatic, non-oliguric transient decline in renal function.[8] Within 24 hours of contrast administration, the serum creatinine begins to rise and usually peaks

Table 1. Laboratory parameters which may be altered in CIN

	Normal range	Alteration
Serum creatinine (SCr)	60–120 µmol/L (0.6–1.5 mg/dL)	↑ 44–220 µmol/L/day (0.5–2.5 mg/dL/day)
Blood urea nitrogen (BUN)	2.5–6.7 mmol/L (8–25 mg/dL)	↑ 3–6.7 mmol/L/day (10–25 mg/dL/day)
BUN: SCr ratio	-	< 15:1
Urinalysis	-	Granular and epithelial cell casts Free epithelial cells Urate, calcium oxalate crystals
Urine osmolality	-	< 350 mOsm/kg
Urinary Na^+ concentration	-	< 30–40 mEq/L*
Fractional Na^+ excretion	-	Usually > 1%**
Bicarbonate	22–30 mmol/L	May ↓
GFR	> 120 ml/min	May ↓
pH	7.35–7.45	May ↓
Potassium	3.5–5 mmol/L	May ↑
Calcium	2.2–2.67 mmol/L (8.5–10.5 mg/dL)	May ↓
Phosphate	0.8–1.5 mmol/L	May ↑

Key: GFR = glomerular filtration rate; Na^+ = sodium; ↑ = increase; ↓ = decrease

* Insensitive index, values overlap between pre-renal and nephrotoxic renal failure

** Fractional Na^+ excretion is typically > 1% in nephrotoxic renal failure although results have been inconsistent with some studies suggesting that Na^+ excretion of < 1% is indicative of CIN[10,11]

Table 2. Reported risk factors for contrast-induced nephropathy

1. **Pre-existing renal impairment**
2. **Diabetes mellitus with renal impairment**
3. **Reduced intravascular volume**
   Congestive cardiac failure
   Diuretics (especially frusemide)
   Abnormal fluid losses
   Liver failure
   Nephrotic syndrome
   Dehydration
4. **Prolonged hypotension**
   Concomitant use of diuretic and ACE inhibitor
   Complication of coronary angiography
5. **Contrast media**
   Large volumes (> 140 ml)
   Repeated injections within 72 hours
   High osmolarity
6. **Diabetes mellitus**
7. **Nephrotoxic drugs**
   e.g. Non-steroidal anti-inflammatory drugs
   Aminoglycosides
8. **Advanced age**
9. **Hypertension**
10. **Proteinuria (including nephrotic syndrome)**
11. **Multiple myeloma**
12. **Hypercholesterolaemia**
13. **Hyperuricaemia**
14. **Hypercalcaemia**
15. **Sepsis**
16. **Atopic allergy**

within 3–5 days, returning to baseline within 10–14 days.[9,10] Oliguric renal failure can occur, typically presenting with oliguria (24-hour urine volume less than 500 ml) within 24 hours of contrast administration, persisting for 2–5 days. Serum creatinine peaks within 5–10 days, returning to baseline within 14–21 days.[11] Of note, morbidity and mortality are significantly higher in this group of patients when compared with those who suffer non-oliguric renal failure.[8]

In patients at high risk, it is recommended that serum creatinine be checked once daily for five days. If an increase is detected, supportive management as an in-patient should be instituted. The patient should be kept under close monitoring until spontaneous recovery of his renal function occurs. Ideally the patient should be transferred to a service with access to facilities for blood purification and fluid removal. Daily assessment of the patient's renal function and serum electrolytes must be performed, as well as careful monitoring of weight and fluid input/output to maintain close control on the patient's fluid and electrolyte balance. Tailored dietary support is essential (see figure 2).

Emergency complications include pulmonary oedema, sepsis and hyperkalaemia. Fluid overload may be treated by diuresis, using loop diuretics, dialysis or haemofiltration as required. Infections must be treated promptly, remembering to avoid nephrotoxic antibiotics. Hyperkalaemia can be corrected by insulin-dextrose infusion if potassium is > 6.5 mmol/L, or by dietary restriction and potassium-binding resins if < 6.5 mmol/L. Hyperphosphataemia can be treated using phosphate binders such as calcium carbonate. The development of a metabolic acidosis may require oral sodium bicarbonate (see figure 2).

More severe cases may require temporary haemodialysis, with a small minority going on to require permanent dialysis or transplantation.[12] Indications for dialysis include uraemic symptoms (anorexia, nausea, vomiting, pruritus, intellectual clouding, drowsiness, fits, coma, haemorrhagic episodes), and complications of uraemia such as pericarditis, hyperkalaemia not controlled by conservative measures, pulmonary oedema or severe acidosis. Some centres recommend prophylactic dialysis if blood urea is greater than 35.7–53.5 mmol/L (100–150 mg/dL) or serum creatinine is greater than 707–884 µmol/L (8–10 mg/dL).

Table 1 shows the various biochemical parameters which may be altered in CIN.

Risk factors

There are numerous proposed risk factors for the development of CIN, many of which are highly prevalent among patients requiring coronary interventional procedures (see table 2). It has been recommended that every known risk factor be analysed to evaluate a total cumulative risk of developing CIN, as total risk rises as the number of risk factors increases.[13,14]

Pre-existing renal impairment

This has been shown to be a significant independent risk factor for the development of CIN. Davidson *et al*. reported a low risk of CIN in patients with normal renal function, but high risk in those with pre-existing azotemia (serum creatinine > 1.2 mg/dL) in a study of 1,144 patients undergoing cardiac catheterisation.[15] Furthermore, they reported that risk increased exponentially with serum creatinine concentration, with a 20% incidence in those with a serum creatinine of 177 µmol/L (2 mg/dL). Likewise Moore *et al*. reported a highly significant relationship between increased baseline serum creatinine levels and frequency of nephrotoxicity. Incidence varied from 2% in those with baseline serum creatinine of < 120 µmol/L (< 1.5 mg/dL) to 20% in those with levels of > 220 µmol/L (2.5 mg/dL).[16]

Reduction of effective intravascular volume

This can be seen in congestive cardiac failure (CCF), dehydration, abnormal fluid losses and liver cirrhosis, for example, and can contribute to pre-renal acute renal failure by reducing renal perfusion, thus enhancing the ischaemic insult of contrast agents.[8,17]

Hypotension

Hypotension, especially when induced by intensive antihypertensive treatment (e.g. combined angiotensin-converting enzyme [ACE] inhibitor and diuretic therapy), can predispose to CIN. Pre-procedural frusemide treatment has been found to be detrimental in a number of studies.[18,19] Similarly, the profound hypotension which can complicate cardiac interventions can result in further renal compromise in patients who are already at risk and who are receiving a considerable contrast load.

Diabetes mellitus

Diabetes mellitus with renal impairment has been identified as an independent risk factor for contrast nephropathy.[20-29]

Diabetes mellitus *per se* without renal involvement has been suggested as being an independent risk factor for CIN. This has not been corroborated by clinical trials.[30]

Contrast media

Volume and osmolarity of contrast, as well as the route of administration (intra-arterial has been shown to be more nephrotoxic than intravenous) also have a direct association with CIN, with large doses[31] and multiple injections of contrast within 72 hours being shown to increase the risk of developing nephropathy.[26,32] The use of low doses of low- or iso-osmolar contrast medium have been shown to reduce the risk of nephropathy substantially in high-risk patients.[8,10,32-36]

Nephrotoxic drugs

These have been implicated as risk factors for the development of CIN. Medications such as cyclosporin A, aminoglycosides, amphotericin and cisplatin directly damage renal tubulo-interstitial cells. Non-steroidal anti-inflammatory drugs (NSAIDs), which act by inhibiting local vasodilatory effects of prostaglandins, have been reported as rendering the kidney more vulnerable to nephrotoxic contrast.[17,28]

Other risk factors

Reduced renal mass, function, and perfusion associated with advancing age have resulted in old age being proposed as a risk factor,[5,26] as has sepsis due to the direct renal tubular damage and impairment of circulation exerted by bacterial toxins.[5] The reported roles of hypertension, peripheral vascular disease,[26] atopic allergy,[32] hyperuricaemia, hypercholesterolaemia, and proteinuria (including multiple myeloma) are neither clear nor well established, although their presence should probably be still taken into account when risk-stratifying patients.

Pathogenesis

The underlying mechanisms of nephrotoxicity are complex as it may involve the interplay of several pathogenic factors.[14,37]

Proposed mechanisms include:

- vasoconstrictive forces resulting in renal medullary ischaemia
- decreased local prostaglandin-mediated vasodilatation, and increased renal adenosine levels
- a direct hypoxic effect on renal tubular cells by contrast media
- damage caused by oxygen-free radicals
- dehydration
- decreased effective intravascular volume.

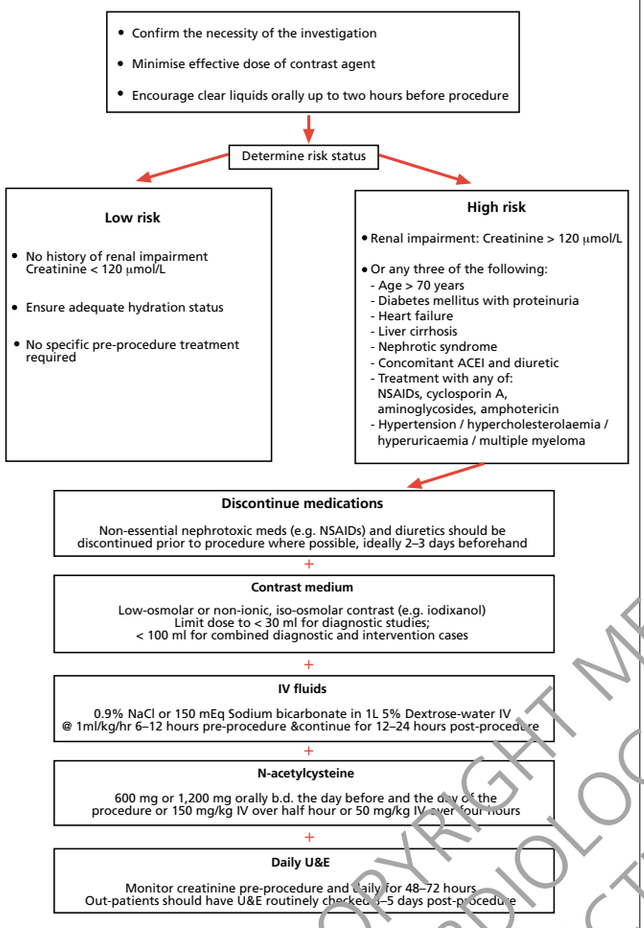
The mechanism most likely to be responsible is thought to be renal tubular ischaemia. Contrast load causes a transient increase in renal blood flow, followed by a more prolonged period of vasoconstriction.[38-41] Imbalance between physiological vasodilator and vasoconstrictive influences mediated by the activity of nitric oxide, prostaglandin and endothelin systems within the medulla are thought responsible.

Consent

Given the increased nephrotoxicity of intra-arterial contrast media, as well as increased rates of diabetes, CCF, hypercholesterolaemia and renal impairment in patients requiring coronary angiography, it is incumbent on the modern cardiologist to ensure risk factors are identified pre-procedure, and that informed consent is obtained. CIN should be included with other potential complications of angiography which are routinely discussed such as haemorrhage, infection, pseudoaneurysm, arrhythmias, etc. Figure 3 gives a rough guide which allows patients to be quickly and easily ranked into those at low risk and those at increased risk.

In the general population, on average, fewer than two in every 100 patients will develop CIN, and the vast majority of these will suffer only transient, asymptomatic decreases in renal function which resolve spontaneously. Patients with a number of

Figure 3. Pre-angiogram protocol to prevent contrast-induced nephropathy



Key: ACEI = angiotensin-converting enzyme inhibitor; NSAIDs = non-steroidal anti-inflammatory drugs; b.d. = twice daily; NaCl = sodium chloride; IV = intravenously; U&E = urea and electrolytes

risk factors should be informed that they are at risk of a deterioration in their kidney function post-procedure, but can be assured that this is mild and transient in almost all patients. A small minority of patients (one in 1,000 in one study) may develop renal failure necessitating renal replacement therapy. Only a small percentage of these go on to need permanent dialysis or kidney transplantation. Patients should realise, however, that should their renal function be grossly impaired, there is an associated increase in post-procedural morbidity and mortality. Every effort should be made to identify those who are at increased risk and to institute pre-procedural preventative measures at an early stage to minimise the risk of development of CIN (see figure 3).

Prevention and treatment

At present, only intravenous (IV) hydration and avoidance of nephrotoxic drugs are universally recognised methods of decreasing the incidence of contrast-induced nephropathy but interest has grown in other pharmacological preventive interventions, most notably in the use of prophylactic N-acetylcysteine.

General measures to minimise the incidence of nephropathy include:

- determining the absolute necessity of the procedure
- use of the minimum effective dose of contrast agent
- abolition of 'nil-by-mouth after midnight' orders in favour of protocols that allow clear liquids up to two hours before procedure.

Other more specific proposed prophylactic measures are outlined below.

Volume expansion

It has been recommended that 0.9% saline by IV infusion at a rate of approximately 1 ml/kg/hr be administered to high-risk patients, adjusted appropriately for the patient's current fluid status and cardiovascular condition. This treatment should be commenced 6–12 hours before the procedure and continued for up to 12–24 hours after the radiographic examination if diuresis is appropriate.[1] Despite its universal acceptance as an effective prophylactic measure, the therapeutic benefit of IV hydration has not been rigorously confirmed in a stringent case-controlled study of significant numbers.

A recent study by Merten *et al*. has produced extremely encouraging results suggesting that the use of sodium bicarbonate hydration is superior to sodium chloride hydration.[42] In this prospective, single-centre randomised trial, 119 patients were administered 154 mEq/L of either sodium chloride or sodium bicarbonate, and it was found that rates of CIN were significantly higher in the sodium chloride group (13.6%, n=8) than in the sodium bicarbonate group (1.7%, n=1). Although the study was limited somewhat by its small sample size, its single-centre nature and its drop-out rates, the authors' argument that bicarbonate is a more efficacious anion than chloride is both logical and attractive, and is backed up by research in animal models. Merten *et al*. suggest that increasing the pH of normal extracellular fluid can inhibit the free-radical formation (which is promoted by an acidic environment) thought to be central in the pathogenesis of CIN. Confirmation of these findings in a larger multi-centre trial is warranted. It seems reasonable in the interim to consider sodium bicarbonate hydration as a safe and effective alternative to normal saline in the pre-hydration of high-risk patients.

Anti-oxidants: N-acetylcysteine

Tepel *et al*. found that the incidence of CIN in patients with chronic renal insufficiency was greatly reduced with N-acetylcysteine (NAC), a thiol-containing antioxidant with vasodilatory properties.[43-45] A dose of 1,200 mg per day, given orally in divided doses on the day prior to and also on the day of administration of the radiocontrast agent, prevented the expected decline in renal function in all patients with moderate renal insufficiency.[45] Incidence of CIN was 21% in the control group versus 2%

in the treated cohort. The study was limited by its low numbers (n=83), lack of long-term follow-up, and the fact that some patients had serum creatinine levels in the normal range.

Similar positive results were reported in other studies[46,47] but several negative or inconclusive studies also exist, most notably Durham *et al*.[48-52] Despite these inconsistencies in findings, an in-depth meta-analysis of seven studies has shown that NAC reduces the occurrence of contrast-induced nephropathy by half in high-risk patients following non-ionic contrast medium administration.[53] Seven trials including 805 patients found NAC plus hydration reduced the relative risk of CIN by 56% (0.435, p=0.02). The meta-analysis may have been adversely affected by the tendency toward publication bias, which may overestimate the true treatment effect, and by the marked heterogeneity among trials analysed.

More recently Briguori *et al*. reported a protective effect of high dose (1,200 mg b.d.) versus standard dose (600 mg b.d.) NAC along with saline hydration in a cohort of 224 patients with chronic renal insufficiency. They also found that the amount of contrast used (greater or less than 140 ml) had a significant effect on outcome.[54]

In a study of 80 patients, however, Goldenberg *et al*. found an incidence of 10% in the NAC group versus 8% in the control group and concluded that prophylactic administration of oral NAC was not justified.[55]

These conflicting reports highlight the point that no definitive benefit has been proven from routine prophylactic therapy with oral NAC. Given its low cost and favourable side-effect profile, its continued use in higher doses in patients with high creatinine levels (> 220 µmol/L [2.5 mg/dL]) receiving large doses of contrast medium (> 140 ml) seems justified.[56] In addition, NAC has been found to reduce composite cardiovascular end points in haemodialysis patients and to reduce the risk of reaching primary end points (fatal and non-fatal myocardial infarction, cardiovascular disease death, need for coronary angioplasty or bypass surgery, ischaemic stroke, or peripheral vascular disease with amputation) by 40% when compared with the control group.[57]

Contrast agents

Low-osmolar contrast medium (LOCM) rather than high-osmolar contrast medium (HOCM) has been shown to be beneficial to patients with pre-existing renal failure but has no advantage in those with normal renal function and no risk factors.[22] Recent studies show a reduced incidence of nephropathy with iodixanol, a new non-ionic, dimeric, iso-osmolar contrast (IOCM).[33]

Although early investigations of iodixanol in low-risk patients failed to show a difference between the frequency of nephropathy when compared with LOCM,[7,58,59] Chalmers and Jackson found iodixanol was less than half as nephrotoxic as the LOCM, iohexol, in 124 consecutive patients with renal impairment undergoing renal and/or peripheral angiography.[60] These findings were confirmed by the NEPHRIC study, a double-blind, randomised, controlled study of 129 patients by Aspelin *et al*. which reported an incidence of CIN of 3% in the IOCM group versus 26% in the LOCM group.[33] The study was limited by the failure to control for volume of contrast administered and by the fact that a higher proportion of patients in the iodixanol group received concomitant ACE inhibitors (78% *vs.* 55%).

The ongoing VALOR study, a multi-centre, randomised trial comparing the renal effects of iodixanol with the LOCM, ioversol, in patients with renal impairment undergoing coronary angiography or interventions, boasts the advantages of being both double-blind and involving a large population.

In a recent trial, iodixanol has also been shown to cause significantly less injection-associated pain and heat sensation than the LOCM iomeprol.[61] In addition, it was shown to cause a smaller vasoconstrictive effect than iopromide and iopamidol,[62] and to have a significantly lower effect on rises in left ventricular end-diastolic pressure when compared to iohexol.[63]

Despite the fact that further data are required, the available evidence suggests that limiting contrast dose and increasing the time interval between procedures (> 72 hours) confers benefit. Dosage should be limited to < 30 ml for diagnostic studies, and < 100 ml for combined diagnostic and percutaneous coronary intervention cases. Some authors recommend a gap of at least 10 days between diagnostic angiogram and complex interventional cases, where possible.[64]

Receptor antagonists

Adenosine antagonists

Three recent studies have suggested that adenosine antagonists may have a role to play in the prevention of contrast-induced nephropathy.[65-67] Theophylline doses of 2.5–5 mg/kg of bodyweight as an IV bolus prior to administration of contrast,[68,69] or orally for three consecutive days prior to radiocontrast injection can be used.[70] These findings contradict earlier studies, which showed inconsistencies in results with theophylline.[71,72] Coupled with its potential side effects, most notably its propensity to cause arrhythmias and convulsions, and its narrow margin between therapeutic and toxic doses,[73] theophylline remains unsuitable for routine prophylactic use. Despite this, it has been suggested that it may still have a role to play in critically ill patients where sufficient hydration may not be possible, as in congestive cardiac failure.[72] Further research is warranted before this potentially toxic drug can be recommended for use as a prophylactic therapy.

Endothelin receptor antagonists

Bosentan, an orally active endothelin antagonist, has been shown to exacerbate radiographic contrast-induced nephrotoxicity.[74]

Diuretics

Diuretics have been shown to have a paradoxically deleterious effect on renal function, especially in diabetic patients,[24,19] and have been shown to exacerbate CIN and increase hospitalisation in those who develop the condition.[18]

Renal vasodilators

Atrial natriuretic peptide (ANP)

ANP, by increasing glomerular filtration rate and glomerular

hydrostatic pressure by dilating afferent arterioles and constricting efferent arterioles while blocking tubular reabsorption of sodium and disrupting the tubuloglomerular feedback mechanism,[1] had been previously reported as reducing the incidence of contrast-induced nephropathy.[75,76] This has since been refuted by several more definitive trials.[24,77,78] ANP is thus no longer recommended for prophylaxis of contrast-induced nephropathy.

Calcium channel blockers

Initially promising results from two studies into the role of calcium as a mediator of contrast-induced nephropathy, which found a benefit to pre-treatment with nitrendipine,[79,80] were contradicted by later studies which found either no benefit, or a deleterious effect, from pre-procedural calcium channel blockers.[18,81,82]

Dopamine

An early report of benefit of dopamine, a potent vasodilator of the renal arteries, found only a small improvement in renal function which was not sustained after day one.[83] Several subsequent studies have shown no benefit.[24,84,85] Recently, the selective dopamine-1-receptor agonist, fenoldopam mesylate, has been shown to be ineffective in CIN prophylaxis.[86]

Prostaglandins

Two studies reported a benefit of pre-treatment with prostaglandin E1 (PGE1) versus placebo but were limited by small numbers, lack of control of hydration status, and type, volume and mode of administration of contrast agent. In addition, a significant number of patients had serious adverse events or a substantial drop in blood pressure during IV infusion. Further large-scale trials with stricter controls are required.[87,88]

Preventive haemodialysis/haemofiltration

A recent study has suggested that peri-procedural haemofiltration given in an intensive care setting may be effective in preventing the deterioration of renal function in patients with chronic renal failure undergoing angiography.[89] By comparison, earlier studies showed no benefit to the removal of contrast medium by haemodialysis.[90,91] The authors suggest the beneficial effects may be due to the haemodynamic stability afforded by haemofiltration in preventing renal hypoperfusion, and the controlled high volume hydration provided. They concede that, because of its cost and its own potential complications, haemofiltration is not suitable for routine prophylaxis. Further definitive trials are warranted in the area.

ACE inhibitors

A report of the benefits of pre-angiogram captopril in CIN prevention by Gupta *et al*. was limited by a lack of a placebo group and small sample size (n=71).[92] In addition, a recent Turkish report found that of a total of 80 patients who underwent coronary angiography, five patients (8.3%) in the captopril group and one patient (3%) in the control group developed CIN. The authors went on to conclude that captopril may even be considered a risk factor for development of CIN.[93]

Key messages

- Identify those at increased risk
- Hydration: N-acetylcysteine – inconsistent results but its use as a prophylactic agent may still be justified pending results of larger multi-centre clinical trials
- Contrast: IOCM – low doses, avoid readministration within 72 hours e.g. iodixanol in high-risk patients

Conclusion

The increasing incidence of CIN requires all clinicians to be both aware of the condition, and to be capable of i) identifying those at risk, ii) instituting preventative measures, and iii) correctly diagnosing and monitoring patients who develop contrast-induced nephropathy.

IV fluids are now standard and although NAC's effectiveness has failed to be confirmed by consistent results in large, randomised clinical trials, its favourable side effect profile, its low cost, and its favourable performance in a recent comprehensive meta-analysis of published research[53] has meant its use is probably justified as a preventative therapy in high-risk patients. Theophylline and prostaglandin therapy remain controversial and require further rigorous evaluation. The role of hydration using sodium bicarbonate also requires further investigation. No other proposed pharmacological therapy has been proven to be of benefit.

Specific measures to be employed in high-risk patients include (see figure 3):

- hospitalisation
- close monitoring of renal function daily for > 72 hours
- discontinuation of nephrotoxic drugs
- IV fluids, and avoidance of dehydration
- NAC, with larger doses (2 x 1,200 mg) being indicated in patients with high creatinine levels (220 µmol/L [> 2.5 mg/dL]) receiving large doses of contrast medium (> 140 ml)
- iso-osmolar contrast medium (e.g. iodixanol)
- limit volume of contrast: < 30 ml in diagnostic angiograms; < 100 ml for combined diagnostic and percutaneous coronary interventions
- delay repeat contrast administration for > 72 hours
- plan delays of > 10 days, or as long as is feasible, between diagnostic studies and complex coronary interventional procedures
- use biplane angiography.

Conflict of interest

None declared.

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