

The K/DIGO, and specifically the “Bone working group”, has made great efforts to evaluate, redefine, classify and update the concept of ‘Renal Osteodystrophy’, a subject highly needed. The position statement from K/DIGO represents an important step forward, to better describe a broader clinical syndrome and a systemic disorder of mineral and bone metabolism secondary to CKD, which implies not only abnormalities in mineral and bone metabolism but also extra-skeletal manifestations. The worldwide adoption of the new recommendations will be useful in clarifying and enhancing international scientific and academic communication in English. However, as mentioned earlier, special efforts must be made in each language to render, this new concept in a few and meaningful words, to convert this new terminology into a handy and useful term to replace ‘Renal Osteodystrophy’.

Conflict of interest statement. None declared.

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Contrast media nephropathy—how to diagnose and how to prevent?

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Introduction

An increasing number of individuals are being exposed to iodinated contrast media (CM). This derives from both the technical advances that have enhanced the role of imaging in the diagnostic and therapeutic arena and the changing demographics of the population. There are more elderly individuals with a burden of chronic diseases including hypertension, diabetes, kidney disease and heart disease, for which the tools of the radiologist and interventionalist are particularly appropriate. It is

therefore not surprising that increasing attention in the medical literature is being given to the renal adverse effect of CM, contrast-induced nephropathy (CIN) and strategies to minimize its incidence.

Before attempting to synthesize from this literature a reasoned approach to the prevention of CIN, I would like to emphasize the pitfalls of this body of work. To begin with, a uniform definition of CIN does not exist. This is no small issue, as the incidence of CIN can vary 2-fold in the same population depending upon whether one uses an *absolute* increase in serum creatinine (≥ 0.5 mg/dl increase) or a *relative* increase in serum creatinine ($\geq 25\%$ increase) or a combination of the two measured 48–72 h post-CM exposure. When a common definition of CIN is not used, comparisons between clinical trials are very difficult. Second, clinical trials in this area tend to be small and single centre (less than a few hundred patients). They often lump together patients with diverse risk factors, routes of CM administration, different types of CM and different reasons for imaging. Particularly in small trials, attempts to adjust for these confounders often lack sufficient power.

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Risk factors

The incidence of CIN increases in patients with certain comorbidities such as impaired kidney function [estimated Glomerular filtration rate (eGFR < 60 ml/min/1.73 m²)], and impaired left ventricular ejection fractions (<40%) [1]. When diabetes is present in addition to one of the above, the incidence of CIN increases further [2]. Based largely upon historical controls and data extolling the benefit of intravenous fluids (see subsequently), patients who are dehydrated or volume-depleted prior to CM administration also have an increased risk of CIN. Finally, any condition that impairs renal blood flow, such as hypotension, or Nonsteroidal anti-inflammatory drugs, is also likely to increase the risk of CIN [3]. Therefore, the first step in designing strategies to minimize the incidence of CIN is to correctly identify those individuals at greatest risk. At the very least, this involves calculating GFR using either the abbreviated modification of diet in renal disease (MDRD) formula or the somewhat less accurate Cockcroft–Gault formula and recording any history of heart failure, diabetes, diuretic use or NSAID use.

Prevention

The next step is to correct any decreases in renal blood flow by ensuring that intravascular volume is replete. This means giving oral saline loading [4] or intravenous fluids in high risk patients and discontinuing diuretics immediately before CM exposure. Many questions remain regarding when to start and for how long to administer intravenous fluids, what type of intravenous fluid to administer and whether the recommendations hold for intravenous as well as intra-arterial administration of CM.

There is a general consensus that for intra-arterial CM studies in high risk patients, intravenous fluids need to be started hours before CM exposure and continued for hours post-CM exposure [5]. Shortening the pre-contrast time for intravenous fluids comes at the expense of a greater rate of administration (up to 3 ml/kg/h for 1 h pre-CM). All the clinical trials involving administration of intravenous fluids have continued the fluids for a minimum of 6 h post-CM at 1 ml/kg/h. There is insufficient data regarding patients at high risk receiving intravenous CM. In a small study of 39 patients, Bader [6] found that intravenous fluids for 12 h before and after CM exposure resulted in a smaller fall in measured GFR and a lower incidence of CIN (5% vs 20%, *P* = NS) compared with a bolus of 300 ml of isotonic saline at the time of CM administration.

The type of intravenous fluids is also controversial. Mueller compared isotonic saline to hypotonic saline in 1620 low-risk patients undergoing cardiac angiography. Intravenous fluids were started on the morning of the angiography and continued at 1 ml/kg/h until

the following morning. Those who received isotonic saline had a lower incidence of CIN (0.7% vs 2.0%). Interestingly, those patients with renal insufficiency did not have a reduction in the incidence of CIN with isotonic saline [7]. Another trial compared isotonic saline with oral water loading in low-risk patients undergoing angiography. Water loading was associated with an increased incidence of CIN compared with intravenous saline (35% vs 4%, respectively) [8]. However, water loading the night before followed by 6 h of intravenous fluids at ≈4 ml/kg/h was as effective as 24 h of intravenous fluids at 1 ml/kg/h in high risk patients undergoing angiography [9]. Isotonic saline has also been compared with isotonic sodium bicarbonate in two trials [10,11]. Both found isotonic bicarbonate to be superior to sodium chloride in patients undergoing cardiac angiography, with and without the addition of N-acetylcysteine [10,11].

Finally, it should be noted that giving intravenous fluids usually increases urine output. However, increasing urine output pharmacologically with furosemide or mannitol has not been uniformly associated with a reduced incidence of CIN. Three prospective randomized trials have found the use of furosemide in addition to intravenous saline to result in a higher incidence of CIN compared with saline alone [4,12,13]. On the other hand, Stevens found that measures to increase urine flow, including mannitol and furosemide, were associated with a decrease in the incidence of CIN in those with urine outputs >150 ml/h [14].

Anti-oxidants

The use of antioxidant derives from our understanding of CIN pathophysiology which highlights the role of reactive oxygen species [15]. The initial demonstration of a protective effect of N-acetylcysteine (NAC) involved patients receiving intravenous CM for abdominal CT exams [16]. Subsequent use of NAC in patients receiving intra-arterial CM found mixed results and a number of meta-analyses could not uniformly support the use of this agent [17]. More recently, trials with higher doses of NAC have been more encouraging [1,18]. A single trial with ascorbic acid also found a benefit in predominately low-risk patients [19] while another trial found no benefit when added to NAC in high-risk patients [11].

Vasodilators

Trials employing vasodilators have produced generally negative results. In some trials, vasodilator-induced systemic hypotension may have contributed to a post procedure rise in serum creatinine unrelated to CM exposure. Current interest has focused on targeted renal therapy (TRT). Vasodilator drug is delivered directly into the renal artery through a special bifurcating catheter placed at the time of angiography. Higher doses of drug can be administered without

systemic side effects [20]. Ongoing trials in high-risk patients will be completed this year.

Choice of contrast media

The dose of CM administered is a generally accepted risk factor for CIN. Dose is best calculated as the ratio of grams of iodine per estimated GFR in millilitre per minute [21]. A meta-analysis comparing high- and low-osmolality CM conducted in the early 1990s found a lower incidence of CIN with low-osmolality CM in patients with chronic kidney disease [22]. A small clinical trial comparing an iso-osmolality CM with a low osmolality CM in high-risk patients also found a lower incidence of CIN with the iso-osmolality agent [23]. These two studies support the concept of 'osmototoxicity' with the lowest incidence of CIN seen when CM with the lowest osmolality are used. However, multiple additional trials comparing iso-osmolality and low-osmolality CM in high-risk populations, with both intravenous and intra-arterial CM, have not been able to confirm these results [24–27]. Rather these trials suggest that CM are nephrotoxic also by virtue of other physiochemical properties and that osmolality alone cannot explain the divergent results [28].

Removal of contrast media

The use of haemodialysis to remove CM following its administration in high risk patients has also been studied. Unfortunately, trials with dialysis concurrent and following CM administration have failed to find any benefit with regard to CIN [29–32]. Dialysis is not able to remove CM quickly enough to prevent the renal injury. In patients with severely impaired renal function (eGFR < 30 ml/min), haemofiltration prior to CM administration is reported to offer protection against both CIN and adverse cardiovascular events [33,34]. However, since the definition of CIN relies on changes in serum creatinine which are lowered by the haemofiltration procedure, it is difficult to conclude that haemofiltration prevents a true fall in GFR.

Summary

The literature leaves much room for continued controversy regarding prevention of CIN. High-risk patients undergoing cardiac or peripheral angiography should receive intravenous fluids for at least 1 h before and 6 h after CM exposure. Sodium bicarbonate may offer an advantage over sodium chloride solutions although more data is required. 'Double dose' NAC may offer better protection than single dose. A minimal dose of a CM with a low incidence of CIN, but not necessarily a low osmolality, should be used.

For patients receiving intravenous CM, including high-risk patients, there is even less data from which to

make recommendations. Patients should be encouraged to drink water starting the day before the exam and, in high-risk patients, additional intravenous saline can be given in the immediate post-procedure period. The efficacy of anti-oxidant therapy needs to be confirmed by additional studies. Low volume of CM with a low incidence of CIN is encouraged.

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Are we overestimating left ventricular abnormalities in end-stage renal disease?

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Introduction

Uraemic cardiomyopathy, defined by the presence of left ventricular hypertrophy (LVH), left ventricular (LV) dilatation or LV systolic dysfunction (LVSD), is reported to be a predictor of premature cardiovascular mortality in patients with end-stage renal disease (ESRD) [1]. Each of these LV abnormalities

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