

Contrast imaging techniques and renal dysfunction

Abstract

Iodinated contrast has been one of the most prescribed and used drugs in contrast imaging techniques and interventional procedures. However, some subjects may develop contrast-induced nephropathy (CIN) especially those in advanced chronic kidney disease (CKD). Diagnostic criterion is based on increasing 48h creatinine after receiving iodine. Given the fact that there is no specific treatment for CIN, prevention should be considered. Uncountable actions should be taken, including: reducing the dose, using a low-osmolar substance, avoiding dehydration and other nephrotoxic drugs. Currently, prevention has been based on using saline solution. A recent paper showed that for patients with stage 3 and 4 of CKD sodium bicarbonate did not provided greater benefit when compared to a saline solution, as well as comparing acetylcysteine to placebo. Regarding to gadolinium, besides nephrotoxicity is irrelevant, there is a risk for developing Nephrogenic Systemic Fibrosis (NSF) which may occur in those with GFR <60mL/min, particularly appears at a GFR <30mL/min. Current gadolinium use guidelines are related to patients with stage 5 (GFR <15mL/min) according to which they should undergo hemodialysis after examination.

Keywords: iodinated contrast, nephrotoxicity, gadolinium, nephrogenic systemic fibrosis, chronic kidney disease

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Abbreviations: CIN, contrast-induced nephropathy; CI-AKI, contrast-induced aki; CKD, chronic kidney disease; Cr, creatinine; GFR, glomerular filtration ratio; NSF, nephrogenic systemic fibrosis; AMI, acute myocardial infarction; NSAIDs, nonsteroidal anti-inflammatory drugs; AKI, acute kidney injury; ATN, acute tubular necrosis; TIN, tubulointerstitial nephritis

Introduction

Iodinated contrast has been one of the most prescribed and used drugs in contrast imaging techniques and interventional procedures. Cancer hospitals frequently use it for diagnosing and staging diseases. Due to clinical complications, such as acute myocardial infarction (AMI) and angina, General hospitals use it for coronary angiography and angioplasty as well as tomography and angiography for those with stroke as a diagnosing and interventionist instrument.

A patient who will receive a contrast approach should be aware of its safety, as well as its risks and clinical benefits for assistance of diagnosed diseases.¹ In this brief review, we are going to discuss how to diagnose and prevent complications related to contrast use such as contrast-induced nephropathy (CIN) and nephrogenic systemic fibrosis (NSF) after using gadolinium.

Discussion

Contrast-induced nephropathy

Frequently, contrast-induced nephropathy (CIN) occurs in advanced stages of chronic kidney disease (CKD) which increases risk of needing a renal replacement therapy (RRT).² Diagnostic criterion is based on increasing 48h creatinine after receiving iodine. Renal biopsy is required only for excluding other causes of acute kidney injury (AKI).³ Given the fact that there is no specific treatment for CIN, prevention should be considered. Uncountable actions should be taken, including: reducing the dose (<200mL), wait longer for repeating exams (>72hours), using a iso or hypoosmolar contrast, avoiding

dehydration during the exam, stopping using nephrotoxic drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) and using periprocedural saline solution.⁴

Dehydration and glomerular filtration ratio (GFR) <60mL/min are the most important risk factor of developing contrast-induced AKI (CI-AKI). However, others morbidities such as diabetes mellitus, cardiac insufficiency and reduction of effective plasma volume as in cirrhosis and in nephrotic syndrome are associated to a greater risk of CIN development.⁴⁻⁶ Besides knowing this frequent cause of AKI it is important in cases of emergency to rank individuals according to the risk of developing CI-AKI as showed in Table 1.

Contrast nephropathy differential diagnosis

Differential diagnosis includes renal atheroembolism, ischemic acute tubular necrosis (ATN), tubulointerstitial nephritis (TIN) and pre-renal AKI after contrast. In people who develops AKI after angiography renal atheroembolism it should be distinguished by presenting at least one of the following characteristics: presence of embolic lesions (digital ischemia) or livedo reticularis, transient eosinophilia or complement consumption, AKI that appears days after being exposed to contrast and long lasting with no recovery of renal function (or low recovery).⁷

Contrast-induced acute kidney injury prevention

Hydration with saline solution 0,9% is possibly the unique way to prevent CI-AKI. However, there are no guidelines regarding do "how much" and "how long". It is suggested to use 1mL/kg/hour of saline solution at least 6hours before the procedure.^{5,6,8}

Bicarbonate hydration protocol may be useful for emergencies especially for the circumstances there are not enough time for hydrating with saline solution. Still, bicarbonate was not more effective in preventing CIN in that cases which RRT was necessary or in cases of death prevention.⁸ Prophylaxis using bicarbonate solution predicts to dilute 150mEq of bicarbonate in 850mL of glucose serum 5%. It

is recommended to use 3.0mL/kg an hour before and, for those who could not take the hydration or who were in emergency condition, 1.0mL/kg 6 hours after the procedure.^{4,6}

Table 1 CI-AKI risk stratification³

	Risk prediction	Risk score	CI-AKI risk	Hemodialysis risk
Hypotension	5			
Intra-aortic balloon pump	5	≤5	7,5 %	0,04%
Congestive heart failure	5			
Age >75anos	4	10-Jun	14%	0,12%
Anemia	3			
Diabetes	3	16-Nov	26,1 %	1,09%
Contrast-media volume	1/ 100ml			
SCr >1,5mg/dl	4	≥16	57,3 %	12,6%
GFR				
40-60mL/min	2			
20-40mL/min	4			
< 20mL/min	6			

Regarding to the contrast substance use, low-osmolar, nonionic substances are safer than high-osmolar ones. Yet, recent papers has not showed that non ionic substances are better than low-osmolar ones.^{6,9} Despite no confirmation of protection through acetylcysteine or bicarbonate hydration⁸ in those individuals with GFR <60mL/min and in emergency cases these strategies could be considered but not without thinking about other approaches. It might be mentioned that there is no evidence of what should be the best prevention strategy.^{4,6,10} Acetylcysteine can be given orally 600mg 12/12hours or, as mentioned by some research 1200mg intravenously 12/12hours.^{11,12}

Recent evidences do not support that statins and vitamin C prevent CIN from happening.² In spite of that a randomized research that evaluated trimetazidine use of 35mg 12/12hours 48h before the contrasted exams for those with GFR between 30 and 90mL/min to take isotonic saline solution 1mL/kg/h and trimetazidine *versus* placebo observed a reduction of CIN incidence in the group that was treated with saline solution and trimetazidine.¹³ Table 2 shows some remarkable strategies for preventing CI-AKI.

Gadolinium contrast

Besides gadolinium has not been related to complications such as AKI for those with previous renal insufficiency, this paramagnetic contrast substance which is used for magnetic resonance exams may develop an incapacitating disease that is not well-known yet. It can progressively affect skin, joints and some organs such as lungs and heart. Its pathophysiological mechanism results from the release of gadolinium especially those from linear molecules from its gadolini-

um-chelate complex that binds to body metals such as iron and zinc. Then, it can be accumulated in skin, joints and organs and may cause progressive tissue fibrosis. First symptoms are skin thickening and pruritus progressing rapidly to contracture and immobility for those who were affected.^{14,15} Among patients who have greater risk for developing Nephrogenic Systemic Fibrosis (NSF) are those with GFR <60mL/min and mainly those with GFR <30mL/min. Table 3 shows risk factors for developing Nephrogenic Systemic Fibrosis (NSF).

Table 2 CI-AKI prevention

To evaluate cost-effective of its benefits.

To evaluate eGFR.

To avoid furosemide 24hours before and after the procedure.

If possible, to avoid nephrotoxic drugs combined with NSAIDs, aminoglycosides.

Hydration with saline solution 0,9% 1mL/kg/h 6-12hours before the procedure and right before it.

Hydration with bicarbonate solution (150mEq bicarbonate/850mL glucose serum 5%) 3,0mL/kg an hour before the procedure and 1,0mL/kg 6hours after it for those who could not take it before and for those who were emergency cases.

To give iso or low-osmolar contrasts and non-ionic substances.

To give the lower possible volume of contrast (<2mL/kg).

To avoid oral hypoglycemic agents during the procedure (risk of hypoglycemia and acidosis in those who may develop AKI).

To recommend 72hours between exams in cases it should be redone.

To give n-acetylcysteine 600mg 12/12h before and after the procedure for those with renal dysfunction (there are controversies).

Table 3 Risk factor for developing nephrogenic systemic fibrosis (NSF)

Patients with stages 4 and 5 of chronic kidney disease (10-13%).

Linear molecules gadolinium.

Gadodiamide (the most related to NSF), and there are some evidences for Gadopentetate and gadoversetamide.

Bigger doses and numerous expositions to the substance.

Erythropoietin use.

Serum iron supplementation.

Patients with vascular disease.

For those who are in dialysis therapy it is recommended to dialyze right after being exposed to contrast (gadobutrol – gadovist) and the two following days after being taking gadolinium (Table 4). Metformin may not be suspended when gadolinium will be used. Current recommendations regarding to gadolinium use shows that just those with end-stage renal disease should dialyze right after the procedure.¹⁶

Table 4 Gadolinium classification manual I**Group 1: Combined agents with a bigger number of NFS cases**

Gadomiamide (Omniscan).

Gadopentetate dimeglumine (Magnevist).

Group 2: Combined agents with a few number of NFS cases or none

Gadobutrol (Gadovist).

Gadoterate Acido (Dotarem).

Group 3: Agents with limited evidence regarding to NFS risk

Gadoxetate dissodio (Eovist).

Conclusion

Besides its frequent use for diagnosing and treating, iodinate contrast may in addition to cause CIN accelerate renal dysfunction and need to RRS and increase treatment costs. Prevention strategies such as hydration with saline solution is important because it reduces further complications. Regarding to the use of gadolinium as a contrast substance the worst effect may happen to those with previous renal dysfunction who use linear molecules. Because it is related to an increased risk of NSF it is recommended to dialyze these patients right after they are exposed to gadolinium.

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Conflict of interest

Author declares that there is no conflict of interest.

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