



Rajul Rastogi*, Prabhat Kumar Bhagat, Yuktika Gupta, Shourya Sharma, Pragya Sinha, Pankaj Kumar Das, Mohini Chaudhary and Vijai Pratap

Teerthanker Mahaveer Medical College and Research Center, Moradabad, UP, India

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***Corresponding author:** Dr. Rajul Rastogi, Assistant Professor, Department of Radiodiagnosis, Teerthanker Mahaveer Medical College & Research Center, Moradabad, Uttar Pradesh, 244001, India, E-mail: eesharastogi@gmail.com

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Review Article

Contrast Induced Nephropathy - A Review

Abstract

In the modern era of widespread utilisation of imaging procedures for preoperative diagnosis and minimal invasive surgeries, intravenous contrast plays a major role in delineation of variety of information related to vascularity of normal as well as abnormal tissues. Vascular structures may themselves be focus of attention for various vascular interventional procedures, again requiring intravenous contrast. Since the intravenous contrast agent used in the imaging procedures is primarily excreted through kidneys, hence pre-procedural renal function should be adequate not only to facilitate its excretion for preventing effects related to contrast retention in body but also contrast-induced nephrotoxicity. As contrast-induced nephropathy is being increasingly encountered in day-to-day practice recently, hence this article focuses on the different facets of contrast-induced nephropathy secondary to iodinated contrast from etiology, risk factors to management.

Introduction

Contrast-induced nephrotoxicity (CIN) refers to sudden deterioration in renal function following the recent intravascular administration of iodinated contrast agent (IoCoAg) in the absence of any another nephrotoxic event. Though, there are no standard criteria for its diagnosis yet percent change in baseline serum creatinine (an increase of 25% to 50%) and absolute elevation from baseline serum creatinine (an increase of 0.5 to 2.0 mg/dL) have been used in the past to indicate CIN. The commonly used criterion is an absolute increase of serum creatinine by 0.5 mg/dL keeping other parameters as method used for estimation and laboratory being constant. CIN is usually asymptomatic with serum creatinine levels reaching peak in 3 to 5 days but in severe oliguric patients, it may take 5 to 7 days to reach a peak.

Acute Kidney Injury (AKI) Network defines acute kidney injury as one of the following occurring within 48 hours after a nephrotoxic event (e.g. intravascular IoCoAg exposure) [1]:

1. Absolute serum creatinine increase of ≥ 0.3 mg/dL (≥ 26.4 μ mol/L).
2. A percentage increase in serum creatinine of ≥ 50 percent (1.5-fold above baseline).
3. Urine output reduced to ≤ 0.5 mL/kg/hour for at least 6 hours.

CIN is the third most common cause of hospital acquired AKI and represent 10–15% of cases [2].

Pathogenesis

Though exact pathophysiology of CIN is not well understood yet following etiologies have been suggested [2]:

- Renal medullary hypoxia secondary to reduced renal perfusion due to renal vasoconstriction (low BP, peripheral vasodilatation) or reduced vasodilators (nitric oxide or prostaglandins).
- Renal glomerular injury manifesting as proteinuria
- Renal tubular injury due to osmolarity, chemotoxicity or ischemia
- Contrast media precipitation of Tamm–Horsfall protein that blocks renal tubules
- Swelling of renal tubular cells causing obstruction
- Both osmotic and chemotoxic mechanisms including agent-specific chemotoxicity

The incidence of CIN in patients with normal renal function is <1 percent with intravenous and 2 to 7 percent with intra-arterial administration of IoCoAg in optimal doses. The higher incidence of CIN in the latter group is not only due to increased incidence of arterial disease in patients requiring such procedures but also due to complications related to catheter-associated procedures. The incidence is approximately up to 16% higher in non-azotemic diabetic patients and up to 33% higher in patients with pre-existent azotemia. Incidence

of 3–16% CIN has been reported in patients undergoing percutaneous coronary interventions as many of these patients have additional risk factors [3–9]. Though AKI is associated with worsened clinical outcome yet current research suggests that is independent of intravenous ICoAg administration due to lack of causal relationship and presence of multiple confounding factors [9].

Risk factors associated with increased incidence of CIN include [2]

- Pre-existing renal impairment (Serum creatinine >1.3mg/dL, GFR <60mL/min)
- Dehydration
- Congestive cardiac failure & use of intra-aortic balloon pumps
- Use of nephrotoxic drugs (NSAID, aminoglycosides)
- Hypersensitivity disease (bronchial asthma)
- Uncontrolled hypertension
- Hyperuricemia (as in active gout)
- Proteinuria (> 0.5 gm/dL)
- Diseases like diabetes mellitus, multiple myeloma, hypoalbuminemia, anemia, hepatic cirrhosis,
- Age > 70 years.

Prevention of contrast induced nephropathy in high risk patients [10–18].

Utilisation of eGFR: It refers to estimation of glomerular filtration rate (eGFR) calculated using the serum creatinine, age, sex and weight of an individual using various formulae. One the commonly used formula is Cockrauff–Gault equation. It is an indicator of the renal function. It has been proved in multiple studies that the risk of CIN with hypo or hyperosmolar iodinated contrast medium is more when the eGFR is less than 50ml/min/1.73m².

Avoidance of iodinated contrast medium: In high-risk patient, the possibility of obtaining the necessary diagnostic information from test not utilising iodinated contrast medium (e.g. ultrasonography, magnetic resonance imaging) must be considered. In some clinical situations, where the use of intravascular iodinated contrast medium may be necessary, lowest possible dose of contrast medium should be used [17,18].

Contrast media selection: Increased osmotic overload on the diseased kidney is considered to be one of the major etiologies of CIN. This can be significantly reduced by substituting LOCM for the very hypertonic HOCM [11]. Isosmolar contrast agent, Iodixanol has recently been introduced which can further minimise renal injury.

Hydration: Adequate hydration is considered to be the single most effective method of preventing CIN. Though, the ideal infusion rate and volume is unknown, yet isotonic fluids

like Ringer lactate or 0.9% normal saline are usually preferred. The American Society of Radiology and the European Society of Urogenital Radiology recommend prophylactic intravenous hydration at the rate of 1.0–1.5ml/kg/hr at least 6 hours prior & after the ICoAg administration in patient at risk of AKI. Oral hydration has also been utilized, but with less demonstrated effectiveness. Pediatric infusion rates are variable and should be based on patient weight [9,10,12].

Sodium bicarbonate: It has been found to be useful in prevention from CIN according to some studies [14,15]. Avoiding concomitant use of nephrotoxic drugs should also be avoided.

Anti-oxidants (N-acetylcysteine & ascorbic acid): Their role is still controversial. However, there is evidence that N-acetylcysteine reduces serum creatinine in normal volunteers without altering Cystatin-C which is a better marker of GFR than serum creatinine. This raises the possibility that N-acetylcysteine might be simply lowering serum creatinine without actually preventing renal injury and should not be considered a substitute for appropriate pre-procedural patient screening and adequate hydration [2,16,17]. Some studies suggest that Allopurinol may have a protective effect in patients with CIN [2].

Hemodialysis and hemofiltration: Their role is controversial in the prevention of CIN even in patients with pre-existing renal diseases [2].

Conclusion

Contrast-induced nephropathy secondary to intravascular, iodinated contrast agent is a commonly encountered clinical condition due to increasing using of various imaging procedures especially in high-risk patients. Though, the risk of CIN is minimal in patients with normal renal function yet caution is needed in patients with serum creatinine >2mg/dL or eGFR < 30mL/min/1.73m². Hydration is the single best protective measure to prevent against CIN. Hence, appropriate knowledge will go a long way in following a balanced approach.

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