Contrast induced nephropathy

Nefropatia induzida por contraste

Authors
Elizabeth Maccariello [1,2,3]

[1] NepHro Consultoria em Doenças Renais, Rio de Janeiro, RJ, Brazil.
[2] Rede D'Or de Hospitais, Rio de Janeiro, RJ, Brazil.
[3] Hospital Universitário Pedro Ernesto, Universidade do Estado do Rio do Janeiro, Rio de Janeiro, RJ, Brazil.

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Correspondence to:
Elizabeth Maccariello.
NepHro Consultoria em Doenças Renais.
Rua Jardim Botânico, nº 674, Sala 405, Rio de Janeiro, RJ, Brazil.
CEP: 22461-000
E-mail: emaccariello@yahoo.com.br

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Iodinated contrast agents are widely prescribed and used in medical practice, and their potential deleterious effects to renal function have been recognized in the literature. Depending on the definition adopted for contrast-induced nephropathy (CIN) and the characteristics of the studied population, the incidence of CIN ranges from 10% to 30%.[1,2]

CIN has been traditionally defined by an absolute increase equal to or greater than 0.5 mg/dl or a relative increase of at least 25% in serum creatinine levels sustained for two to five days in the absence of other identifiable causes starting within 48 to 72 hours of the intravenous administration of an iodinated contrast agent. Historically, the diagnoses of CIN and contrast-associated acute kidney injury (CA-AKI) have been confused; while CIN presupposes causality, CA-AKI may signify CIN or AKI concomitant to the use of iodinated contrast instead of caused by it. The vast majority of published clinical studies use the two terms interchangeably and do not include control groups in their series, which raises questions over the actual incidence of CIN and the acute and chronic impacts on kidney function introduced by the use of iodinated contrast agents.

In recent years, the diagnosis of CIN has been revisited in prospective controlled clinical trials designed to better understand this potentially preventable cause of AKI. In a meta-analysis, McDonald *et al.*[3] found only 13 controlled studies from a total of 1489, including 25,950 patients. The incidence of AKI, prescription of dialysis, and death rates were similar in the groups given iodinated contrast or not. In a controlled prospective observational study, Hemmett *et al.*[4] reported an incidence of AKI of about 11% in 843 inpatients. However, the incidence of AKI was similar in the group given contrast and in the group not given intravenous iodinated contrast. Recent data show that CIN is rarely seen in patients with an estimated glomerular filtration rate (eGFR) greater than 45 ml/min/1.73m^2, although stage IV and V chronic kidney disease is one of the main risk factors for the development of CIN.[1,5,6]

Other risk factors for CIN include: diabetes; congestive heart failure; age over 70 years; hypovolemia; concomitant use of nephrotoxic agents and non-steroidal anti-inflammatory drugs.[1,2]

The clinical diagnosis of CIN and accurate determination of risk factors remain challenging in clinical practice, and the pathophysiology of the condition is still not thoroughly understood. Most of the mechanisms described are derived from experimental models that are unable to accurately represent the disease's clinical manifestations. Nonetheless, they are required for a better understanding of CIN, and offer insight into possible ways of preventing the condition and curtailing its long-term deleterious effects.

And to clarify some of the aspects pertaining to the pathophysiology of CIN affecting different groups of the population, study "*Impact of gender in early structural changes of contrast induced nephropathy in rats*" de Carraro-Eduardo *et al.*[7], is a more than welcome

addition to the collection of papers published in this issue of the *Brazilian Journal of Nephrology*.

The authors showed, corroborating the literature, that the intravenous administration of hyperosmolar iodinated contrast to nephrectomized Wistar rats deprived of water results in early structural kidney damage, observed through significant increases in proximal renal tubule cell vacuolation, thus raising three important questions:[7]

1 - The animal model, albeit adequate according to the literature, relies on pre-sensitization by unilateral nephrectomy and water deprivation. Is there is a parallel between the need for pre-sensitization in the CIN experimental model and recent data in the literature that consider CIN to be a rare condition in patients with an eGFR above 45 ml/min/1.73m^2 without the other risk factors?[1,5]

2 - Did the type of contrast - hyperosmolar - used in the study affect the observed results? In Wistar rats, the intravenous injection of contrast agents with similar physicochemical characteristics may cause different intensity and duration changes;[8] however, contrast hyperosmolarity plays a key role in the survival, growth, and proliferation of cultivated human proximal renal tubule epithelial cells.[9] In clinical practice, although the advantages of using low-osmolar and iso-osmolar contrast medium in individuals with a normal GFR have been discussed, these agents have been broadly used to mitigate the adverse effects of osmolarity in renal hemodynamics, particularly in groups at risk of developing CIN.[1,10]

3 - The study was designed to look into early structural damage, but can injury persist for longer? What is the likelihood of these injuries becoming chronic?

Finally, the study shows that female Wistar rats are significantly more susceptible to injury when given intravenous hyperosmolar iodinated contrast agents. This finding echoes with some observational studies in which female gender was an independent risk factor for CA-AKI,[11] although this evidence was not categorized as highly relevant.

The study sheds light on important points and offers insight into points pertaining to the pathophysiology of CIN and its clinical impact on renal function that call for additional investigation. It also takes us a step further toward the safer use of intravascular iodinated contrast and the larger goal of offering relevant information on the use of contrast agents in clinical practice.

References

1. Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int 2006;(100):S11-5.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int 2012;2:1-138.
3. McDonald JS, McDonald RJ, Comin J, Williamson EE, Katzberg RW, Murad MH, et al. Frequency of acute kidney injury following intravenous contrast medium administration: a systematic review and meta-analysis. Radiology 2013;267:119-28. PMID: 23319662 DOI:http://dx.doi.org/10.1148/radiol.12121460
4. Hemmett J, Er L, Chiu HH, Cheung C, Djurdjev O, Levin A. Time to revisit the problem of CIN? The low incidence of acute kidney injury with and without contrast in hospitalized patients: an observational cohort study. Can J Kidney Health Dis 2015;2:38. DOI:http://dx.doi.org/10.1186/s40697-015-0073-6
5. Davemport MS, Khalatbari S, Dillman J, Cohan RH, Caoili EM, Ellis JH. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material. Radiology 2013;267:94-105. doi: 10.1148/radiol.12121394.
6. Davenport MS, Khalatbari S, Cohan RH, Dillman JR, Myles JD, Ellis JH. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: risk stratification by using estimated glomerular filtration rate. Radiology 2013;268:719-28. DOI:http://dx.doi.org/10.1148/radiol.13122276
7. Carraro-Eduardo JC, Macedo HW, Silva LE. Impact of gender in early structural changes of contrast induced nephropathy in rats. J Bras Nefrol 2016;38:383-8.
8. Tervahartiala P, Kivisaari L, Kivisaari R, Vehmas T, Virtanen I. Structural changes in the renal proximal tubular cells induced by iodinated contrast media. PMID: 9171307
9. Andreucci M, Faga T, Russo D, Bertucci B, Tamburrini O, Pisani A, et al. Differential activation of signaling pathways by low-osmolar and iso-osmolar radiocontrast agents in human renal proximal tubular cells. J Cell Biochem 2014;115:281-9. DOI: http://dx.doi.org/10.1002/jcb.24662
10. 10. Barrett BJ, Carlisle EJ. Meta-analysis of the relative nephrotoxicity of PMID: 8511292 high- and low-osmolality iodinated contrast media. Radiology 1993;188:171-8. PMID: 8511292
11. Iakovou I, Dangas G, Mehran R, Lansky AJ, Ashby DT, Fahy M, et al. Impact of gender on the incidence and outcome of contrast-induced nephropathy after percutaneus coronary intervention. J Invasive Cardiol 2003;15:18-22.