Selected Summaries

Prophylactic hydration to protect renal function from intravascular iodinated contrast material

Nijssen EC, Rennenberg RJ, Nelemans PJ, Essers BA, Janssen MM, Vermeeren MA, van Ommen V, Wildberger JE. (Departments of Radiology and Nuclear Medicine, Internal Medicine, Epidemiology, Clinical Epidemiology and Medical Technology Assessment, and Cardiology, Maastricht University Medical Centre, Maastricht, The Netherlands.) Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): A prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. *Lancet* 2017;**389:**1312–22.

SUMMARY

The 'A MAstricht Contrast-Induced Nephropathy Guideline' (AMACING) trial was a prospective phase 3 randomized, single-institute, parallel-group, open-label, non-inferiority trial designed to assess the utility of intravenous hydration for prophylaxis of patients at risk of developing contrast-induced nephropathy (CIN). Adult high-risk patients with an estimated glomerular filtration rate (eGFR) of 30–59 ml/minute/1.73 m^2 who would be receiving intravenous or intra-arterial contrast were enrolled, and were randomized to receive standard intravenous saline as prophylaxis versus no prophylaxis. The incidence of CIN was compared between the two groups, with a non-inferiority margin set at 2.1%.

The trial was performed between June 2014 and July 2016. Exclusion criteria included eGFR <30 ml/minute/1.73 m^2, patients on renal replacement therapy, intensive care patients, and emergency cases. The randomized patients were stratified on the basis of eGFR (<45 *v.* ≥45 ml/minute/1.73 m^2), presence or absence of diabetes, intravenous or intra-arterial contrast administration, and diagnostic or interventional study. After exclusion, consecutive patients were enrolled on either the hydration arm (328 patients) or the no prophylaxis arm (332 patients). The incidence of CIN was not statistically different in the two groups (2.7% *v.* 2.6% respectively; 8 in each arm). No haemodialysis, intensive care admission, or related mortality occurred in either arm on a 35-day follow-up. Eighteen patients in the hydration arm developed hydration-related complications. No prophylaxis was observed to be non-inferior and significantly more cost-effective compared to intravenous saline, predominantly due to hospitalization costs, in patients at risk of CIN.

COMMENT

CIN prophylaxis and its efficacy have always been shrouded in uncertainty. Various options for prophylaxis include volume expansion with oral or intravenous hydration with normal saline, use of intravenous sodium bicarbonate, use of N-acetylcysteine, and use of iso-osmolar contrast medium, among others.[1–3] The benefit of oral hydration or intravenous saline was not established beyond doubt before this trial; however, being relatively cheap and safe to use, it is considered to be the minimum standard of care as per the current American College of Radiology (ACR) guidelines.[1,2] Data and meta-analysis available on other prophylactic measures are conflicting, and the current evidence is not sufficient to recommend them.[1,2]

Most previous studies compared one mode of CIN prophylaxis with another, with very few randomized studies comparing hydration with no prophylaxis.[4–6] Two studies included patients with ST elevation myocardial infarction receiving intra-arterial contrast (coronary angiography).[4,6] The patients in the two studies were randomized to receive intravenous normal saline versus no hydration and compared for the incidence of CIN, and hydration was found to be superior. However, a majority of patients in these studies had normal renal function. Extrapolating these results to intravenous contrast administration is not appropriate, as there are many other confounders with intra-arterial administration.[2] A third study comparing sodium bicarbonate with no hydration in patients with eGFR <60 ml/minute/1.73 m^2 undergoing CT pulmonary angiography (receiving intravenous contrast) observed that no hydration was not inferior to hydration with sodium bicarbonate.[5] Given that the use of sodium bicarbonate was not the standard hydration regimen, the current study compared no hydration with intravenous hydration with normal saline in patients with eGFR of 30–59 ml/minute/1.73 m^2, and found no hydration to be non-inferior.

The results of Nijssen *et al.*'s study are along expected lines, as recent literature has indicated that intravenous contrast is not an independent risk factor for acute kidney injury in patients with eGFR ≥30 ml/minute/1.73 m^2.[2,7–11] Since contrast-induced nephropathy was unlikely to happen in patients enrolled in the study (all with eGFR 30–59 ml/minute/1.73 m^2), it is hardly surprising that the prophylaxis against CIN did not help. However, this study does add substantially to our understanding because the recent literature on CIN is retrospective and many patients must have received some form of prophylaxis. Thus, Nijssen *et al.*'s work re-emphasizes that it is safe to administer intravenous contrast in patients with eGFR ≥30 ml/minute/1.73 m^2 by addressing this limitation. Recent literature also suggests that contrast may not be an independent risk factor for kidney injury even in patients with eGFR <30 ml/minute/1.73 m^2, and it would be worth doing a similar study in this subgroup as well.[9,10]

Will this study change practice? The current widely practised minimum standard of care remains hydration, but this study reinforces the growing belief that even this may not be needed at all in patients who do not have severe chronic renal impairment. However, long-held beliefs and practices are unlikely to change quickly. This study will make clinicians and radiologists more comfortable in avoiding intravenous hydration, particularly in patients who are critically ill, or those who have a potential volume overload, or require emergency contrast-enhanced CT, as well as perhaps in outpatient settings, where no hydration (or oral hydration) should suffice.

In summary, Nijssen *et al.*'s trial, taken in conjunction with the recent literature on CIN, suggests that it is safe and cheaper to administer intravenous contrast in patients with eGFR ≥30 ml/minute/1.73 m^2 without prophylaxis.

REFERENCES

1 Manual on Contrast Media v10.2. Available at *www.acr.org/Quality-Safety/Resources/Contrast-Manual* (accessed on 3 Apr 2017).

2 Davenport MS, Cohan RH, Ellis JH. Contrast media controversies in 2015: Imaging patients with renal impairment or risk of contrast reaction. *AJR Am J Roentgenol* 2015;**204:**1174–81.

3 ESUR Contrast Media Guidelines version 8.1. Available at *www.esur.org/guidelines/* (accessed on 3 Apr 2017).
4 Jurado-Roman A, Hernandez-Hernandez F, Garcia-Tejada J, Granda-Nistal C, Molina J, Velázquez M, *et al*. Role of hydration in contrast-induced nephropathy in patients who underwent primary percutaneous coronary intervention. *Am J Cardiol* 2015;**115:**1174–8.
5 Kooiman J, Sijpkens YW, van Buren M, Groeneveld JH, Ramai SR, van der Molen AJ, *et al*. Randomised trial of no hydration vs. sodium bicarbonate hydration in patients with chronic kidney disease undergoing acute computed tomography-pulmonary angiography. *J Thromb Haemost* 2014;**12:**1658–66.
6 Luo Y, Wang X, Ye Z, Lai Y, Yao Y, Li J, *et al*. Remedial hydration reduces the incidence of contrast-induced nephropathy and short-term adverse events in patients with ST-segment elevation myocardial infarction: A single-center, randomized trial. *Intern Med* 2014;**53:**2265–72.
7 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
8 Hinson JS, Ehmann MR, Fine DM, Fishman EK, Toerper MF, Rothman RE, *et al*. Risk of acute kidney injury after intravenous contrast media administration. *Ann Emerg Med* 2017;**69:**577–86.e4.
9 McDonald JS, McDonald RJ, Carter RE, Katzberg RW, Kallmes DF, Williamson EE. Risk of intravenous contrast material-mediated acute kidney injury: A propensity score-matched study stratified by baseline-estimated glomerular filtration rate. *Radiology* 2014;**271:**65–73.
10 McDonald RJ, McDonald JS, Newhouse JH, Davenport MS. Controversies in contrast material-induced acute kidney injury: Closing in on the truth? *Radiology* 2015;**277:**627–32.
11 Wilhelm-Leen E, Montez-Rath ME, Chertow G. Estimating the risk of radiocontrast-associated nephropathy. *J Am Soc Nephrol* 2017;**28:**653–59.

AKSHAY D. BAHETI
Department of Radiology
Tata Memorial Hospital
Mumbai
Maharashtra

BHAVIN JANKHARIA
Picture This by Jankharia
Mumbai
Maharashtra
bhavin@jankharia.com