НИРКИ ПОЧКИ KIDNEYS

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D.D. Ivanov
Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine

Contrast-induced nephropathy: searching for new solutions to prevent its development

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Abstract. *Contrast-induced nephropathy (CIN) is the main cause of acute kidney injury and worsens the prognosis of chronic kidney disease. To evaluate the clinical risk score of CIN development, various medical calculators are proposed. The main criterion for assessing the possible development of CIN is the initial glomerular filtration rate presented by estimated glomerular filtration rate. Toxic effect of contrast substances is realized through the properties of the molecule of contrast itself (tubular cell damage) and induced ischemia with oxidative stress and vasoconstriction. Existing methods for preventing the development of CIN are based on reducing the toxic effect of a contrast agent and preventing hypoxic kidney shock. The drugs currently proposed are acetylcysteine, statins, and some other approaches as well as hemodialysis. However, the evidence base is the most informative for hydration, which should be used before the introduction of a contrast agent, along with the minimization of the dose of contrast. Nevertheless, no final solution has been found to prevent the development of CIN. We have proposed the use of edaravone, which has an evidence base for ischemic stroke, to prevent the development of CIN. Three patients with chronic kidney disease stage 3b were given 30 mg edaravone twice a day before contrast media infusion and during two days after contrast administration. In two patients, CIN was avoided. The proposed approach requires future research to evaluate its effectiveness.*

Keywords: *contrast-induced nephropathy; hydration; chronic kidney disease; edaravone*

Contrast-induced nephropathy (CIN) is the major cause of acute kidney injury in chronic kidney disease (CKD) [1] and a third most common cause of acute kidney injury (AKI) in hospitalized patients following volume depletion and medication [2].

Contrast-induced nephropathy is defined as the impairment of renal function measured as either a 25% increase in serum creatinine from baseline or a 0.5 mg/dL (44 μmol/L) increase in absolute serum creatinine value within 48–72 hours after intravenous contrast administration [3].

For evaluation of percutaneous coronary intervention (PCI) risk, the following calculators are recommended: https://bmc2.org/calculators/multi and https://bmc2.org/calculators/cin for CIN risk calculation in particular [4].

Several guidelines provide CIN patient surveillance; one of the latest (2018) is represented by the European Society of Urogenital Radiology (ESUR) [5] that defines post-contrast acute kidney injury as an increase in serum creatinine ≥ 0.3 mg/dl (or ≥ 26.5 μmol/l), or ≥ 1.5 times from baseline, within 48–72 h of intravascular administration of contrast medium (CM).

The key recommendations of this guideline are the following:

1. Nephrotoxic medication

In CKD patients receiving CM, optimal nephrology care involves minimizing the use of nephrotoxic drugs (level of evidence A).

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers do not have to be stopped before CM administration (level of evidence D).

There is insufficient evidence to recommend withholding nephrotoxic drugs such as nonsteroidal anti-inflammatory drugs, antimicrobial agents or chemotherapeutic agents before CM administration (level of evidence B).

Для кореспонденції: Іванов Дмитро Дмитрович, доктор медичних наук, професор, завідувач кафедри нефрології і нирково-замісної терапії, Національна медична академія післядипломної освіти імені П.Л. Шупика, вул. Дорогожицька, 9, м. Київ, 04112, Україна; e-mail: drivanovdd@gmail.com
For correspondence: Dmytro D. Ivanov, MD, PhD, Professor, Head of the Department of nephrology and renal replacement therapy, Shupyk National Medical Academy of Postgraduate Education, Dorohozhytska st., 9, Kyiv, 04112, Ukraine; e-mail: drivanovdd@gmail.com
Full list of author information is available at the end of the article.

Table 1. Management of CIN prevention

Glomerular filtration rate, mL/min	Management
≥ 60–90	Conduction of the study with preventive actions
≥ 45–60	Assessment of study necessity
≥ 30–45	According to vital signs
Less than 30	No study is conducted

2. Hydration

Preventive hydration should be used to reduce the incidence of post-contrast acute kidney injury in patients at risk (level of evidence B).

Intravenous saline and bicarbonate protocols have similar efficacy for hydration (level of evidence A).

For intravenous and intra-arterial CM administration with the second pass renal exposure, hydrate the patient with either: a) 3 mL/kg/h 1.4% bicarbonate (or 154 mmol/L solution) for 1 h before CM; or b) 1 mL/kg/h 0.9% saline for 3–4 h before and 4–6 h after CM (level of evidence D).

For intra-arterial CM administration with the first pass renal exposure, hydrate the patient with either: a) 3 mL/kg/h 1.4% bicarbonate (or 154 mmol/L solution) for 1 h before CM followed by 1 mL/kg/h 1.4% bicarbonate (or 154 mmol/L) for 4–6 h after CM; or b) 1 mL/kg/h 0.9% saline for 3–4 h before and 4–6 h after CM (level of evidence D).

Oral hydration as the sole means of prevention is not recommended (level of evidence D).

No other drug recommendations (acetylcysteine, statins) and dialysis for CIN prevention were presented in the guidelines; it is associated with their poor evidential base. However, a positive effect of nebivolol that is used to reduce the risk of CIN and is prescribed before contrast study was not evaluated [6].

An important aspect is also the absence of the need to prescribe diuretics both in CIN and in acute kidney injury (see below) [7].

Difference in diuretics management in AKI and CKD

1. Sudden stop of diuresis:

— acute kidney injury: diuretics are contraindicated, euvolemia maintenance is recommended.

2. Chronic fluid retention:

— chronic kidney disease: long-term diuretic therapy is indicated (loop diuretics and aldosterone antagonists), vascular hypovolemia should be avoided.

Before deciding to perform PCI, our clinic has chosen the following algorithm (Table 1).

Therefore, **nowadays the only method of CIN prevention is hydration** [5, 8], and risks are determined by glomerular filtration rate and by the state of the cardiovascular system.

Toxic effect of contrast substances is realized through:

1) properties of the molecule of contrast itself (tubular cell damage);

2) induced ischemia with oxidative stress and vasoconstriction [9].

Serum creatinine levels peaking 2–3 days after administration of contrast medium and returning to baseline within 7–10 days after administration are accompanied by ischemic changes [10].

While evaluating CIN pathogenesis, our attention was paid to another aspect about ischemia — the successful use of edaravone, an agent blocking the ischemic cascade; nowadays, it is used for treatment of acute ischemic stroke [11]. It is to be recalled some facts about edaravone:

— this agent was involved in clinical studies with a high level of evidence that have been conducted in Japan since 2001;

— every third patient having received the drug during the first 24 hours after onset of ischemia will have no consequence of stroke at all;

— this is the first drug over the past 23 years that is approved by the Food and Drug Administration in 2017 for treatment of amyotrophic lateral sclerosis [12].

In our clinic, three patients with stage 3b CKD have received 30 mg of edaravone (Xavron, Ukraine) intravenously twice a day before PCI and two days after the procedure. Development of CIN was observed in one patient; two patients have shown less than a 1.5-fold increase in serum creatinine level during 5 days of monitoring.

We believe that the initiation of use of **edaravone for CIN prevention** provides a clinical perspective. Nevertheless, future trials need to be done to prove the possibility of preventing CIN with edaravone.

Conflicts of interests. The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. *National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002 Feb;39(2 Suppl 1):S1-266.*

2. *Jeon J, Kim S, Yoo H, et al. Risk Prediction for Contrast-Induced Nephropathy in Cancer Patients Undergoing Computed Tomography under Preventive Measures. J Oncol. 2019 Apr 1;2019:8736163. doi: 10.1155/2019/8736163.*

3. *Kellum JA, Lameire, Aspelin P, et al. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kindey Int. 2012;2(1):1-138. doi:10.1038/kisup.2012.1.*

4. *Gurm HS, Seth M, Kooiman J, Share D. A novel tool for reliable and accurate prediction of renal complications in patients undergoing percutaneous coronary intervention. J Am Coll Cardiol. 2013 Jun 4;61(22):2242-8. doi: 10.1016/j.jacc.2013.03.026.*

5. *Van der Molen AJ, Reimer P, Dekkers IA, et al. Post-contrast acute kidney injury. Part 2: risk stratification, role of hydration and other prophylactic measures, patients taking metformin and chronic dialysis patients : Recommendations for updated ESUR Contrast Medium Safety Committee guidelines. Eur Radiol. 2018 Jul;28(7):2856-2869. doi: 10.1007/s00330-017-5247-4.*

6. Shamekhi Amiri F. Recent advances in the treatment of renal diseases with nebivolol: A literature review. Nephrol Ther. 2016 Jun;12(3):140-8. doi: 10.1016/j.nephro.2016.01.011.

7. Ivanov DD, Rostaing L. Diuretics and advanced features of nephroprotection. Počki. 2019;8(1):2-6. doi: 10.22141/2307-1257.8.1.2019.157790. (in Russian).

8. Maioli M, Toso A, Leoncini M, et al. Bioimpedance-Guided Hydration for the Prevention of Contrast-Induced Kidney Injury: The HYDRA Study. J Am Coll Cardiol. 2018 Jun 26;71(25):2880-2889. doi: 10.1016/j.jacc.2018.04.022.

9. Yang J, Peng Y, Tsai S, et al. The molecular mechanism of contrast-induced nephropathy (CIN) and its link to in vitro studies on iodinated contrast media (CM). Biomedicine (Taipei). 2018 Mar;8(1):1. doi: 10.1051/bmdcn/2018080101.

10. Hossain MA, Costanzo E, Cosentino J, et al. Contrast-induced nephropathy: Pathophysiology, risk factors, and prevention. Saudi J Kidney Dis Transpl. 2018 Jan-Feb;29(1):1-9. doi: 10.4103/1319-2442.225199.

11. Enomoto M, Endo A, Yatsushige H, Fushimi K, Otomo Y. Clinical Effects of Early Edaravone Use in Acute Ischemic Stroke Patients Treated by Endovascular Reperfusion Therapy. Stroke. 2019 Mar;50(3):652-658. doi: 10.1161/STROKEAHA.118.023815.

12. Watanabe K, Tanaka M, Yuki S, Hirai M, Yamamoto Y. How is edaravone effective against acute ischemic stroke and amyotrophic lateral sclerosis? J Clin Biochem Nutr. 2018 Jan;62(1):20-38. doi: 10.3164/jcbn.17-62.

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Information about author

Dmytro D. Ivanov, MD, PhD, Professor, Head of the Department of nephrology and renal replacement therapy, Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine; e-mail: drivanovdd@gmail.com; ORCID iD: orcid.org/0000-0003-2609-0051

Иванов Д.Д.
Национальная медицинская академия последипломного образования имени П.Л. Шупика, г. Киев, Украина

Контраст-индуцированная нефропатия: поиск новых решений для предотвращения ее развития

Резюме. Контраст-индуцированная нефропатия (КИН) является основной причиной острого повреждения почек и ухудшает прогноз хронической болезни почек. Для определения клинического риска развития КИН предлагаются различные медицинские калькуляторы. Основным критерием оценки возможного развития КИН является начальная скорость клубочковой фильтрации, представленная расчетной скоростью клубочковой фильтрации. Токсическое действие контрастных веществ реализуется через свойства самой молекулы контраста (повреждение тубулярных клеток) и посредством индуцированной ишемии с окислительным стрессом и вазоконстрикцией. Существующие методы предотвращения развития КИН основываются на снижении токсического действия контрастного вещества и предотвращении гипоксического почечного шока. В настоящее время предложено применение ацетилцистеина, статинов, некоторых других подходов, например гемодиализа. Однако доказательная база является наиболее информативной в отношении гидратации, которую следует использовать перед введением контрастного вещества наряду с минимизацией дозы контраста. Тем не менее достоверных рекомендаций по снижению КИН не разработано. Мы предложили использовать эдаравон, который имеет доказательную базу при ишемическом инсульте, для предотвращения развития КИН. Три пациента с хронической болезнью почек стадии 3b получали по 30 мг эдаравона 2 раза в день перед инфузией контрастного вещества и в течение двух дней после введения контраста. У двух пациентов развития КИН удалось избежать. Предложенный подход требует дальнейших исследований для оценки его эффективности.

Ключевые слова: контраст-индуцированная нефропатия; гидратация; хроническая болезнь почек; эдаравон

Іванов Д.Д.
Національна медична академія післядипломної освіти імені П.Л. Шупика, м. Київ, Україна

Контраст-індукована нефропатія: пошук нових рішень для запобігання її розвитку

Резюме. Контраст-індукована нефропатія (КІН) є основною причиною гострого ураження нирок і погіршує прогноз хронічної хвороби нирок. Для визначення клінічного ризику розвитку КІН пропонуються різні медичні калькулятори. Основним критерієм оцінки можливого розвитку КІН є початкова швидкість клубочкової фільтрації, представлена розрахунковою швидкістю клубочкової фільтрації. Токсичний ефект контрастних речовин реалізується через властивості самої молекули контрасту (пошкодження тубулярних клітин) і шляхом індукованої ішемії з окислювальним стресом і вазоконстрикцією. Існуючі методи запобігання розвитку КІН ґрунтуються на зниженні токсичної дії контрастної речовини і запобіганні гіпоксичному нирковому шоку. На даний час запропоноване застосування ацетилцистеїну, статинів, деяких інших підходів, наприклад гемодіалізу. Однак доказова база є найбільш інформативною щодо гідратації, яку слід використовувати перед введенням контрастної речовини разом із мінімізацією дози контрасту. Однак вірогідних рекомендацій щодо зниження КІН не розроблено. Ми запропонували застосовувати едаравон, що має доказову базу за ішемічного інсульту, для запобігання розвитку КІН. Три пацієнти з хронічною хворобою нирок стадії 3b отримували по 30 мг едаравону 2 рази на день перед інфузією контрастної речовини і протягом двох днів після введення контрасту. У двох пацієнтів розвитку КІН вдалося уникнути. Запропонований підхід вимагає подальших досліджень для оцінки його ефективності.

Ключові слова: контраст-індукована нефропатія; гідратація; хронічна хвороба нирок; едаравон