

Prevention and Management of Adverse Reactions Induced by Iodinated Contrast Media

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Abstract

Iodinated radiocontrast media (IRCM) is widely used in current clinical practice. Although IRCM is generally safe, serious adverse drug reactions (ADRs) may still occur. IRCM-induced ADRs may be subdivided into chemotoxic and hypersensitivity reactions. Several factors have been shown to be associated with an increased risk of ADRs, including previous contrast media reactions, history of asthma and allergic disease, etc. Contrast media with lower osmolality is generally recommended for at-risk patients to prevent ADRs. Current premedication prophylaxis in at-risk patients may reduce the risk of ADRs. However, there is still a lack of consensus on the prophylactic role of premedication. Contrast-induced nephropathy (CIN) is another component of IRCM-related ADRs. Hydration remains the mainstay of CIN prophylaxis in at-risk patients. Despite several preventive measures, ADRs may still occur. Treatment strategies for potential contrast reactions are also summarised in this article. This article summarises the pathophysiology, epidemiology and risk factors of ADRs with emphasis on prevention and treatment strategies. This will allow readers to understand the rationale behind appropriate patient preparation for diagnostic imaging involving IRCM.

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Introduction

Since the introduction of the first iodinated radiocontrast media (IRCM) by Dr Moses Swick in 1929, it has been widely used in a variety of radiological examinations, with more than 50 million studies performed per year.^{1,2}

Iodine is the core element in radiocontrast media, which is required in certain amounts to provide adequate film-screen radio-opacity.³ The design of the contrast media aims to maximise the amount of iodine atoms to ensure the image quality and to minimise the osmolality in order to reduce toxicity.⁴

There are 4 types of IRCMs: ionic monomers, ionic dimers, non-ionic monomers and non-ionic dimers (Table 1). The ionic monomers such as diatrizoate (Urografin) and iothalamate (Conray) were introduced in 1950 to 1960 and were considered high osmolar ionic contrast media (HOCM), with the highest osmolality of 1500 mOsm/kg. Osmolality

was subsequently reduced by dimerisation of monomers and by producing non-ionic contrast media. Non-ionic monomers (metrizamide) were first introduced in 1969 by Dr Torsten Almén with a much lower osmolality (around 600 mOsm/kg) compared to the former. Newer non-ionic monomers such as iohexol or iopamidol were developed in 2006 and are more stable and less toxic. Ioxaglate (Hexabrix) is one of the ionic dimers with osmolality of 560 mOsm/kg and was first introduced into the United States in the 1980s. Because of the lower osmolality nature of non-ionic monomers and ionic dimers, these contrast media are categorised as low osmolar contrast media (LOCM). Non-ionic dimers (e.g. iodixanol, iotrolan) are the most recently developed IRCM. These contrast agents possess the lowest osmolality and are physiologically isotonic (300 mOsm/kg, the origin of the term iso-osmolar contrast media, IOCM).^{2,3} Currently, iohexol (Omnipaque 350) is used in almost all the major hospitals in Singapore as contrast

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Table 1. Comparison of Iodinated Radiocontrast Media*

Types	Examples	Osmolality (mOsm/kg)
Ionic monomer (HOCM)	Diatrizoate	1500
	Iothalamate	
	Metrizamide	
Non-ionic monomer (LOCM)	Iohexol	600 – 800
	Iopamidol	
	Ioversol	
Ionic dimer (LOCM)	Ioxaglate	560
Non-ionic dimer (IOCM)	Iodixanol	300
	Iotrolan	

*Source: McClellan BL, Preston M. Hickey memorial lecture. Ionic and nonionic iodinated contrast media: evolution and strategies for use. *AJR Am J Roentgenol* 1990;155:225-33; and Grainger RG. Intravascular radiological iodinated contrast media. In: Grainger & Allison's Diagnostic Radiology. 5th ed. Elsevier Churchill Livingstone; 2007.

media for enhanced computed tomography (CT) studies and intravenous urograms. Omnipaque 350 has osmolality of 844 mOsm/kg and is one of the non-ionic LOCM. Another commonly used IRCM in Singapore is ioversol (Optiray), which is a non-ionic LOCM with lower osmolality (502 to 792 mOsm/kg) and associated with lower risk of reactions. This contrast agent is more frequently used for inpatient settings.

Various adverse drug reactions (ADRs) to IRCM are published in the literature. The reaction spectrum is wide, ranging from rash to anaphylaxis.⁵ The introduction of LOCM has significantly decreased the incidence of ADRs.⁵ Although most of the ADRs are mild and almost self-limiting, severe reactions do occur and could be life-threatening.⁶ Therefore, it is crucial for both radiologists and referring physicians to keep updated with information on IRCM-related ADRs. In our institution, prednisolone is prescribed prior to contrast injection to prevent possible reactions for patients with asthma, multiple drug allergies (>3 drugs) and previous contrast reactions. Moreover, oral or intravenous hydration is recommended prior to contrast injection to prevent contrast-induced nephropathy.

There are 4 major international guidelines addressing this topic: European Society of Urogenital Radiology Contrast Media Safety Committee guidelines (ESURCMSC) version 8.1, American College of Radiology (ACR) Manual on Contrast Media version 9 and Standards for Intravascular Contrast Agent Administration to Adult Patients by the Royal College of Radiologists (RCR) Second Edition 2010 and Consensus Guidelines for the Prevention of Contrast Induced Nephropathy by Canadian Association of Radiologists (CAR) 2011. This article reviews and summarises these guidelines and relevant articles in PubMed to provide practitioners with a comprehensive overview on this topic.

Table 2. Adverse Reactions of Iodinated Radiocontrast Media

Reactions	Chemotoxic Reactions	Hypersensitivity Reactions	
		Acute	Late
		Mild:	Skin reactions:
	Nausea		
	Vomiting	Itching, erythema	Urticaria
	Flushing	Urticaria	Persistent rash
	Arrhythmia	Moderate:	Steven-Johnson syndrome*
	Pulmonary edema	Bronchospasm	
	Seizure	Angioedema	
	Renal toxicity	Severe:	
	Vasovagal attacks	Anaphylaxis	

*Source: Savill JS, Barrie R, Ghosh S, Muhlemann M, Dawson P, Pusey CD. Fatal Stevens-Johnson syndrome following urography with iopamidol in systemic lupus erythematosus. *Postgrad Med J* 1988;64:392-4.

Classification and Pathophysiology of Adverse Reactions

In general, ADRs of IRCM are classified based on the severity and timing of symptoms⁷ and the underlying pathophysiology.^{6,8} However, the classification system of ADRs is diverse and lack universal consensus. In this article, we adopt the classification system of the ACR guidelines, which is based on pathophysiology and onset timing of clinical presentation.

Chemotoxic or Physiologic Reactions

Chemotoxic reactions, also known as physiologic reactions, are ADRs caused directly by the physiochemical effect of the IRCM.⁹ Hyperosmolality, the binding ability of IRCM with calcium ions and the concentration of IRCM's cations are believed to play an important role in the pathogenesis of chemotoxic reactions.⁹ Mild chemotoxic reactions usually manifest as warmth, nausea, vomiting or flushing. Severe reactions may be related to organ toxicity, such as arrhythmia, pulmonary edema, seizure or renal toxicity^{6,9-11} (Table 2).

Vasovagal reactions are classified under this category in the ACR guidelines.⁶ Increased vagal tone from the central nervous system depresses and inhibits the cardiac conduction system. Therefore, patients who have vasovagal reactions may present with combined hypotension and bradycardia.^{6,9}

Hypersensitivity Reactions

Hypersensitivity reactions (HRs) are also known as allergic-like, pseudoallergic or anaphylactoid reactions in the literature. Different from chemotoxic reactions, the

incidence and severity of HRs are independent of the dose and injection rate of IRCM.¹² HRs are further divided into acute (within 1 hour) and late reactions (from 1 hour to days).^{13,14}

Symptoms of acute HRs include urticaria, erythema, angioedema, bronchospasm, laryngeal edema and anaphylactic shock^{5,9,13} (Table 2). The underlying pathogenesis is dominated by non Ig-E mediated anaphylactoid reactions.¹⁵ These reactions are mediated by direct IRCM-activation of mast cells and basophils, activation of coagulation/kinin system and complement cascades.¹⁶ Nevertheless, Ig-E mediated allergic reactions may also play a role in the acute HRs as reported in several studies.¹⁷⁻¹⁹

Late HRs are usually mild to moderate in severity and self-limiting. Despite various reported late HRs, the majority of symptoms consist of skin manifestations²⁰ (Table 2). Late skin reactions are believed to be related to T cell-mediated allergic reactions, which are similar to most of the drug-related skin reactions.^{20,21} The awareness of this subset of delayed allergy reaction among radiologists is important in the process of patient counselling on the aftercare of the use of IRCM.

Epidemiology

Acute Adverse/Hypersensitivity Reactions

The actual prevalence of acute ADR is difficult to assess.⁶ A few factors may affect the prevalence of ADRs, such as the physiochemical property of IRCM and premedication.¹⁶ Generally, patients receiving HOCM are at higher risk of developing acute reactions (mild: 5% to 15%, moderate: 1% to 2% and severe: 0.2%) compared to LOCM (mild: 3%, moderate: 0.2% to 0.4% and severe: 0.04%).¹⁴ The introduction of LOCM has significantly reduced the non-fatal adverse events. However, the incidence of rare mortality is similar between HOCM and LOCM (1:170,000).^{22,23}

The prevalence of acute ADRs in patients receiving IOCM is similar compared to LOCM. In one observational study, acute ADR rate was reported as 0.3% and severe ADR rate as 0.05% after intravenous administration of iodixanol.²⁴

The ACR, RCR and ESUR guidelines identify previous hypersensitivity reactions (especially moderate to severe), asthma and allergic disease (multiple severe allergies or allergy disease requiring treatment) as substantial risk factors for acute HRs^{6,7,25} (Table 3).

Previous allergic reaction to IRCM is the most important risk factor with a recurrence rate ranging from 10% to 35%.⁶ A study by Katayama et al supported this fact, with the highest reported incidence of ADRs coming from patients with previous acute HRs to IRCM.⁵

Asthmatic patients are at an increased risk of severe ADR

Table 3. Risk Factors of Hypersensitivity Reactions

	Acute Hypersensitivity Reactions	Chronic Hypersensitivity Reactions
Risk Factors	Previous acute HRs	Previous late HRs
	Asthma	Allergic disease
	Allergic disease	Iso-osmolar dimer
	Old age*	Women, Japanese descent†
	Medical treatment of beta-blocker‡	Systemic disease, such as SLE IL2 treatment

HRs: Hypersensitivity reactions; IL-2: Interleukin-2; SLE: Systemic lupus erythematosus

*Source: Cashman JD, McCredie J, Henry DA. Intravenous contrast media: use and associated mortality. *Med J Aust* 1991;155:618-23.

†Source: Bellin MF, Stacul F, Webb JA, Thomsen HS, Morcos SK, Almen T, et al. Late adverse reactions to intravascular iodine based contrast media: an update. *Eur Radiol* 2011;21:2305-10.

‡Source: Lang DM, Alpern MB, Visintainer PF, Smith ST. Elevated risk of anaphylactoid reaction from radiographic contrast media is associated with both beta-blocker exposure and cardiovascular disorders. *Arch Intern Med* 1993;153:2033-40.

by 10 folds with intravenous HOCM injection and by 6 folds with non-ionic LOCM or IOCM injection.^{5,25} Among the subgroups of atopic diseases, asthmatic patients have the highest risk of developing severe HRs.⁵

Multiple allergies or a single severe allergy requiring treatment is another risk factor for acute HRs.^{7,25} Katayama et al has demonstrated that there was an increased risk of overall ADRs, with 3 folds severe reaction in patients of prior history of allergy.⁵ Notably, the risk of ADR in patients with seafood allergy is not significantly higher than other allergic disease.^{15,26} Therefore, seafood allergy is not considered as an independent risk factor.⁶

Late Hypersensitivity Reactions

According to the ACR guidelines, the incidence of late hypersensitivity reaction ranges from 0.5% to 14%.^{6,27,28}

Iso-osmolar dimer is associated with a higher incidence of late ADR compared with other IRCMs.²⁰ History of allergy and previous late reactions are the other substantial risk factors^{14,20} (Table 3).

Patients of systemic diseases such as systemic lupus erythematosus (SLE) are more prone to develop late reactions.^{20,29,30} Besides, there is a 2 to 4 folds increased risk of late reactions among patients receiving IL-2 immunotherapy^{6,20} (Table 3).

Prevention of Hypersensitivity Reactions

Prevention of Acute Hypersensitivity Reactions

Life threatening IRCM-induced HRs are rare. A systemic review assessed the effectiveness of applying premedication

in general population. The result was not cost-effective due to a large number needed to treat to prevent one potential severe life threatening reaction.³¹ Therefore, current practice mainly focuses on at-risk patients only.

Premedication in At-Risk Patients

The underlying pathophysiology of acute HRs following IRCM has been discussed earlier. It is believed that the allergic-like reactions secondary to IRCM are induced by histamine and other mediators released by activated basophils and eosinophils.¹⁶ In a study conducted by Dunskey et al, corticosteroids demonstrated significant suppression effect on the number of these circulating immune cells. The effect reached statistical significance at 4-hour and peaked at 8-hour.³² This finding explains the basis of premedication, at least 4 hours prior to the IRCM administration.^{6,33,34}

A series of studies have been carried out to gather evidence on the efficacy of steroid prophylaxis in clinical circumstances. In the first place, steroids are unable to provide prophylaxis if given immediately prior to the administration of IRCM.^{35,36} Nevertheless, multidose regimen with 1 dose given at least 4 hours prior to IRCM that dominates current clinical practice has been advocated in a few studies. Lasser et al applied a 2-dose regimen of methylprednisolone 32 mg per oral (PO) (one dose 6 hours and the other 2 hours prior to the contrast administration). The results showed significant reduction in overall acute HRs and severe reactions in patients who received HOCM injections.³⁶ Another randomised study in 1994 was performed in patients who received non-ionic LOCM. The result again showed the 2-dose regimen conferred significant protection in overall and mild reactions. However, the reduction in severe reactions has not achieved statistical significance.³⁴

In the current ACR guidelines, premedication for at-risk patients is not routinely recommended, in view of the lack of solid evidence to support the effects on severe reaction prevention.⁶ However, several premedication regimens are still recognised for potential prophylactic effects.⁶ In the clinical setting of elective premedication, the ACR

guidelines list 2 commonly used regimens (Table 4):

- 1. Prednisolone 50 mg PO at 13-hour, 7-hour and 1-hour before contrast media injection + diphenhydramine 50 mg IV, IM or PO 1-hour before contrast media.
- 2. Methylprednisolone 32 mg PO at 12-hour and 2-hour before contrast media +/- antihistamine.

For emergency premedication, methylprednisolone sodium succinate 40 mg or hydrocortisone sodium succinate 200 mg IV q4h until contrast study + diphenhydramine 50 mg IV 1-hour before contrast injection is proposed by the ACR guidelines⁶ (Table 4).

Both ESUR and RCR guidelines state that there is not enough evidence to confirm the effectiveness of premedication. However, if the premedication is deemed to be used, the suggested regimen in the ESUR guidelines is prednisolone 30 mg (or methylprednisolone 32 mg) PO at 12-hour and 2-hour before contrast media⁷ (Table 4).

It is worth emphasising that premedication doesn't prevent chemotoxic reactions due to different underlying pathophysiology.

Selection of IRCM to Prevent Acute HRs

The osmolality of IRCM has been shown to be positively correlated with histamine release in basic scientific study.³⁷ A study by Katayama et al built up more clinical evidence on the application of non-ionic LOCM in practice. They reported a significant reduction of overall ADRs in the group of non-ionic LOCM compared to the HOCM.⁵ However, there is still a lack of well organised studies to demonstrate the preventive role of LOCM in severe life threatening ADRs.¹²

Based on these evidence, the ACR guidelines clearly state that the safety margin of LOCM is better than HOCM.⁶ In the ESUR guidelines, HOCM is categorised as an independent risk factor for acute ADRs and non-ionic LOCM is recommended in every patient.⁷ The RCR guidelines also suggest that high risk patients should receive non-ionic LOCM or IOCM, if administration of IRCM is deemed necessary.²⁵

Table 4. Premedication Regimens

Guidelines		Regimen
ACR guidelines	General	Prednisolone 50 mg PO at 13-hour, 7-hour and 1-hour before contrast media injection + diphenhydramine 50 mg IV, IM or PO 1-hour before contrast media
		Methylprednisolone 32 mg PO at 12-hour and 2-hour before contrast media +/- antihistamine
	Emergency	Methylprednisolone 40 mg IV or hydrocortisone 200 mg IV q4h until contrast study + diphenhydramine 50 mg IV 1-hour before contrast media
ESUR guidelines	Prednisolone 30 mg PO or methylprednisolone 32 mg PO at 12-hour and 2-hour before contrast media	

ACR: American College of Radiology; ESUR: European Society of Urogenital Radiology; IM: Intramuscular injection; IV: Intravenous injection; PO: Per oral

Previous Hypersensitivity to IRCM

Previous hypersensitivity reaction to IRCM is the most important risk factor for recurrent allergic-like reactions. Despite the use of premedication, breakthrough reactions after IRCM administration may still occur.^{38,39} Davenport et al conducted a study to analyse the frequency and severity of breakthrough reactions after LOCM injection in premedicated patients with history of contrast media allergies.³⁹ It showed that 81% of the breakthrough reactions were of similar severity to the prior ones. In patients with previous breakthrough reactions, only 12% of the subsequent LOCM injections resulted in recurrent reactions. Risk factors associated with severe breakthrough reactions include chronic oral corticosteroid use, drug or severe allergies and multiple allergies to 4 or more allergens.³⁹

The effectiveness of using a different IRCM agent to prevent recurrent reactions has not been fully established.^{13,39,40} However, both RCR and ESUR guidelines suggest using a different non-ionic LOCM or IOCM, if injection of IRCM is necessary.^{7,25}

Asthma Patients and Patients with Severe Atopic Disease

Asthmatic patients are at higher risk of developing acute HRs after IRCM administration. However, evidence shows that treated asthma doesn't add extra risk compared to the general population.⁴¹ Therefore, the RCR guidelines advise that the premise of proceeding with contrast study is to ensure that the patient's asthma status is under control. If the asthma is poorly controlled and the study is not urgent, the procedure should be rescheduled until asthma status is stabilised.

The type and severity of allergy should be clarified before proceeding with contrast injection. If the patient has severe allergy or multiple allergies, radiologists should consider the risks and benefits of a contrast study and look for other alternative imaging studies without using IRCM.²⁵

Both RCR and ESUR guidelines recommend non-ionic LOCM or IOCM in patients having asthma, multiple allergies or severe allergy requiring treatment. In addition, patients should be monitored for 30 minutes after the procedure and medical staff in the radiology department should be ready to treat any ADRs.^{7,25}

Prevention of Late Hypersensitive Reactions

Late HRs are usually mild in severity and self-limiting. No special instruction is needed for patients without risk factors.²⁰

For patients with known history of late HRs, no solid evidence is reported to support the utility of corticosteroid and antihistamine to prevent recurrent late HRs.^{6,42} Due to

the rarity of severe late HRs, drug prophylaxis is generally not recommended.^{6,7} However, in our institution, we will still counsel the patient on the existence of this subset of delayed allergy reaction as part of the process of holistic informed consent. The patients will be educated on appropriate action plan at home if any of the allergy reactions occur or worsen.

The ESUR guidelines recommend using the intradermal test to confirm the contrast agent that leads to late HRs and to study cross-reactivity to other IRCMs. In order to reduce the risk of recurrent late HRs, another IRCM without cross-reactivity may be considered. On the other hand, IRCMs that demonstrated cross-reactivity on intradermal tests should be avoided.^{7,20}

Contrast-Induced Nephropathy (CIN): Preventive Measures

Besides hypersensitivity reactions, contrast-induced nephropathy (CIN) is another important IRCM-induced ADR. CIN is defined as a deterioration of renal function (defined as increase in serum creatinine by more than 25% or 44 $\mu\text{mol/l}$) within 3 days of intravascular administration of IRCM in the absence of an alternative aetiology.⁷

Risk factors associated with increased CIN risks are summarised in Table 5.⁴³ Renal impairment is by far the most important predictor of CIN.^{6,43,44} It increases the risk of CIN by more than 20 times.^{6,45} Conventionally, the threshold of eGFR is 60 mL/min. However, in the updated ESUR guidelines, the precautionous cutoff level has been lowered from eGFR <60 mL/min to eGFR <45 mL/min.^{7,43} This is because data and review of the intravenous IRCM administration studies showed that the risk of CIN increases only if eGFR is <45 mL/min.⁴⁶

Fluid volume expansion and avoidance of dehydration are the main measures to prevent CIN.^{43,47} Nephrotoxic drugs should be stopped for at least 24 to 48 hours after discussing with the referring clinician, for example non-steroid anti-inflammatory drugs.⁷

To reduce the risk of CIN, the majority of guidelines recommend the use of LOCM, for example iohexol, or IOCM, for example iodixanol.^{6,7,25,43,44}

After contrast-enhanced imaging studies are performed, volume expansion therapy should be continued and eGFR values at 48 to 72 hours after should be obtained.^{7,43}

Treatment of Adverse Reactions

Despite the use of LOCM and premedication, ADRs may still occur in a sporadic and unpredicted manner. All guidelines emphasise on well equipped preparation for any possible ADRs.^{6,7,25} Prompt management requires early recognition, well trained medical staff and easy access to

Table 5. Risk Factors for CIN*

1. Patient-Related Risk Factors
Renal impairment is the most important predictor
Diabetic nephropathy
Congestive heart failure
Dehydration
Age >70 years
Anaemia
Concurrent use of nephrotoxic drugs
Known or suspected acute kidney injury
Cardiovascular instability
2. Procedure-Related Risk Factors
Intra-arterial administration
High osmolality contrast media
Large doses of contrast media
Multiple administrations within a few days interval

*Source: European Society of Urogenital Radiology contrast media Safety Committee guidelines; and Leow KS, Wu YW, Tan CH. Renal-related adverse effects of intravenous contrast media in computed tomography. Singapore Med J 2015;56:186-93.

resuscitation facilities.⁶

It is important to evaluate patients’ allergic signs and symptoms before planning further treatment. Symptoms, conscious level, vital signs, skin appearance, auscultation and phonation should be assessed, followed by determination of the severity of reactions.⁶

In the case of acute cardiopulmonary collapse, the American Heart Association Advanced Cardiac Life Support (AHA ACLS) guidelines should be followed. Treatment strategies for specific reactions, such as urticaria, bronchospasm, laryngeal edema, hypotension and vagal reaction, are advised by main international guidelines and summarised in Table 6.^{6,7,25}

In contrary to the RCR and ESUR guidelines, ACR guidelines proposed the use of adrenaline 1:10000, 0.3 mg IV (up to total 1 mg) in hypotensive patients, reason being the poor perfusion to the extremity in hypotensive patients may decrease the absorption rate of adrenaline via intramuscular injection.⁶ In our local practice, we think this approach is reasonable and preferred.

Late reactions are usually self-limiting and require no specific therapy except for symptomatic treatments such as antihistamines and corticosteroids.^{6,25} If symptoms are prolonged or progressively worsening, referral to allergic specialists for further management should be considered.⁶

Table 6. Treatments for Adverse Contrast Reactions

Signs and Symptoms		Treatments
Nausea/vomiting		Supportive treatment Anti-emetic for severe cases
Urticaria/erythema		Supportive treatment Adrenaline 1:1000, 0.1 – 0.3 mg IM for severe cases
Bronchospasm	Normotensive	O ₂ supply and beta-2 agonist Adrenaline 1:1000, 0.1 – 0.3 mg IM
	Hypotensive	O ₂ supply and beta-2 agonist Adrenaline 1:1000, 0.5 mg IM
Laryngeal edema		O ₂ supply and beta-2 agonist Adrenaline 1:1000, 0.5 mg IM
Isolated hypotension		Elevation of legs, O ₂ supply and intravenous fluid challenging Adrenaline 1:1000, 0.5 mg IM
Vasovagal reaction		Elevation of legs, O ₂ supply and intravenous fluid challenging Atropine 0.6 – 1.0 mg IV (up to total 3 mg)
Acute cardiopulmonary collapse		Follow the American Heart Association Advanced Cardiac Life Support guidelines
Late reactions		Supportive treatments

ACR guidelines: adrenaline 1:10000, 0.3 mg IV (up to total 1 mg) for hypotensive patients
ACR: American College of Radiology; IM: Intramuscular injection; IV: Intravenous injection; O₂: Oxygen

Conclusion

ADRs to IRCM are divided into chemotoxic and hypersensitivity reactions based on the underlying pathophysiology. There are several factors associated with an increased risk of ADRs, such as previous contrast media reactions, history of asthma, allergic disease and Interleukin-2 (IL2) therapy, etc.

Non-ionic LOCM and IOCM are generally recommended in at-risk patients. Premedication is routinely employed in clinical practice, and may be helpful to reduce mild acute HRs. However, there is no conclusive evidence available to support its prophylactic efficacy in severe ADRs. Late reaction is normally mild and self-limiting, hence no preventive procedure is needed.

In patients receiving intravenous IRCM administration, the previously accepted threshold of eGFR <60 mL/min has been lowered to eGFR <45 mL/min, whilst the threshold of <60 mL/min remains for intra-arterial IRCM administration. To reduce risk of CIN, hydration is the most important measure to prevent CIN in at-risk group, and it should be continued into the postprocedural period.

Despite the use of non-ionic IRCM and premedication, severe life-threatening ADRs may still occur. Therefore, the risk and benefits of IRCM must be balanced with consideration of possible alternatives. Radiologists and clinicians must be well prepared to treat any ADRs promptly with standby emergency drugs and equipment.

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