

Preventing recurrent hypersensitivity reactions to iodinated contrast media

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Iodinated contrast media (ICM) is one of the most commonly used drugs in the practice of modern medicine. ICM, as the name implies, is a contrast media that contains iodine. It is frequently used in computed tomography (CT) and angiographic procedures, to highlight important anatomical structures and for the detection of pathologies. While most ICMs are administered by radiology practices, other specialties such as cardiology and gastroenterology also use them to guide angiography and some endoscopic procedures.

They are currently many different ICMs in the market. Those which are used as intravenous or intrathecal agents are low osmolality contrast media or iso-osmolality contrast media agents. Common examples include iohexol (Omnipaque, GE HealthCare, Chicago, IL, US), iopromide (Ultravist, Bayer, Berlin, Germany) and iodixanol (Visipaque, GE HealthCare, Chicago, IL, US). High osmolality contrast media such as diatrizoate sodium/meglumine (Gastrografin, Bracco Diagnostics, Milan, Italy) are older generation agents, which are associated with a higher rate of adverse events. They are now generally used for only gastrointestinal and cystourethral administrations.

While ICM is generally safe to use, it is estimated that 0.6% of patients who received ICM will suffer an “allergic-like” or hypersensitivity reaction. A frequently used classification system for hypersensitivity reactions is by the American College of Radiology, which categorises the reactions as mild (limited urticaria, pruritis, nasal congestion), moderate (generalised urticaria/oedema, voice hoarseness without dyspnea, wheezing without hypoxia) and severe (severe oedema, respiratory distress, circulatory collapse).

Severe hypersensitivity reactions are rare, occurring in 4 in 10,000 patients. Patients who develop a hypersensitivity reaction to ICM are deemed to be at significant risk for a recurrent reaction.¹ For patients who had a previous non-severe reaction and require a repeat administration of ICM, it is currently common practice to pre-medicate them with corticosteroids as a prophylactic measure.

The article by Wong et al.² is timely as the study brings to our attention how ICM hypersensitivity reactions

can be misunderstood by medical practitioners. It also highlights the emerging trends in prevention strategy.

Common misconceptions and the importance for appropriate documentation. It is commonly thought that a patient who developed a hypersensitivity reaction to ICM must have an allergy to iodine. While patients can be allergic to povidone iodine (a surface antiseptic), allergy to elemental iodine does not exist. After all, iodine is an essential nutrient required for the synthesis of the thyroid hormones. It is also commonly present in an everyday ingested condiment, the table salt. Another common misconception is that seafood allergy is associated with significant ICM hypersensitivity. Again, this is not true as the major allergens, parvalbumins in fish and tropomyosins in shellfish are unrelated to iodine.³ Patients with allergies to povidone iodine and seafood allergies are actually not at greater risk from ICM than patients with other types of allergies.¹

Wong et al. highlighted in their study, a high portion of non-specific, incomplete or misleading information in their patients’ ICM hypersensitivity records. Their experience mirrors commonly encountered situations in many radiology practices in Singapore. For example, it is not uncommon to come across patients who were simply documented as having an allergy to “computed tomography (CT) contrast”. This is akin to labelling a patient who had a hypersensitivity reaction to penicillin as having an “antibiotic allergy”—an important but ultimately limited piece of information. It is also not uncommon that the severity of the reactions is not described in detail. Perhaps, such practices may have been consequential from the misconceptions that have been described earlier. As Wong et al. have demonstrated, switching to a different ICM is now a viable strategy for patients with prior non-severe hypersensitivity reactions to ICM. It is therefore pertinent to re-iterate the need for accurate documentation when one encounters a patient who develops a reaction.

Firstly, it is highly recommended that the documentation and drug alert labelling of a witnessed reaction in the electronic medical records (EMR) be made by a firsthand witness rather than a secondhand account. A

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firsthand account will likely be the most accurate and least ambiguous. In most scenarios when the reaction is acute, the firsthand account should originate from the supervising radiologist or the proceduralist who administered the ICM, rather than the physician or clinical team who manages the patient. Secondly, it is important to recognise and differentiate the severity of the witnessed episode. Description of patient's signs and symptoms should be as accurate as possible. While assessment can admittedly be subjective or challenging to differentiate between a hypersensitivity reaction and a chemotoxic physiological effect, the use of a standard classification such as that by ACR is helpful to reduce variability. Thirdly, it is important to name the specific ICM that had caused the hypersensitivity reaction. These details, when available will allow us to accurately risk stratify the patient and prescribe the appropriate preventive measures.

Emerging trends in prevention strategies. In North America and Singapore, it remains common to offer corticosteroids, with or without antihistamines to patients who are at risk of developing a hypersensitivity reaction to contrast media. However, this is not without controversy. While there is good evidence that corticosteroid prophylaxis prevents aggregate and mild hypersensitivity reaction to low osmolality contrast media in average-risk patients, there is no best data or level 1 evidence confirming that they are equally effective in preventing reactions in higher-risk patients (i.e. patients who had previous ICM hypersensitivity).⁴ In addition, breakthrough contrast hypersensitivity reactions can occur in pre-medicated patients. The reported breakthrough rate is 2.1%; in most cases of about 81%, breakthrough reaction is similar in severity to the index reaction.¹ The use of corticosteroids does not come with negligible risks. They may result in transient hyperglycaemia and leucocytosis. However, more often than not, it is non-compliance, which is a greater issue. Patients who do not take their pre-medication may end up not receiving their scheduled CT scan on time, potentially leading to a delay in critical diagnosis.

Changing to a different ICM is a strategy that has been gaining traction. There is emerging evidence that doing so may be more effective than pre-medication. A recent large scale Korean prospective study with 196,081 recruited patients demonstrated that a change of ICM can reduce the risk of recurrent hypersensitivity reaction.⁵ In fact, the European Society of Urogenital Radiology (ESUR) has went as far as recommending a change of ICM in lieu of corticosteroid pre-medication in their guidelines.⁶

Given these emerging trends, it is not inconceivable that the use of pre-medication prophylaxis may not be necessary in the foreseeable future or that a combination of changing ICM and use of pre-medication will become a standard. It is important that users of ICM look into how this may affect their departmental workflow. For example, there will be a need to ensure sufficient supplies and stocks on a variety of ICMs. It may also be necessary to look into cost-efficient methods to ensure that a patient's ICM hypersensitivity records can be easily documented in standard formats, retrieved and reviewed from the EMR. Wong et al. has given us examples of workflow adjustments to accommodate these new strategies in their department.

Lastly, direct referral services to an allergist are no doubt a helpful initiative. ESUR recommends that patients who had a previous ICM hypersensitivity reaction preferably consult an allergist, before using a different contrast agent. While it may not be feasible for some practices to refer all ICM hypersensitivity cases, the allergist can serve an important role, particularly in managing patients with ambiguous ICM records. It will be helpful for departments to work with their allergy services on the appropriate referral guidelines.

Prevention strategies for recurrent ICM hypersensitivities are evolving, with emerging evidence that a change of ICM may be preferred when compared to just the use of pre-medication prophylaxis. Accurate documentation of patients' ICM hypersensitivity reactions is an important tenet. Users of ICM should keep abreast with the latest recommended practice guidelines and redesign departmental workflows where necessary.

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