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Real incidence and management of patients with suspected iodinated contrast media allergy in our area

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Abstract
Introduction: Adverse reactions to iodinated contrast media (ICM) are very common due to its widespread use. Despite the fact that overall incidence of hypersensitivity reactions (HSRs) to ICM is low, the risk of severe outcomes needs a careful patient evaluation and management.
Methods: We conducted a retrospective epidemiological study that included patients referred to our Allergy Unit for suspected allergy to ICM in whom we carried out a protocolized allergic study based on skin and drug provocation tests (DPT).
Results: A total of 108 patients were tested and allergy to ICM was confirmed in 29 (26.9%) and assumed in 9 (8.3%). All these patients tolerated DPT with alternative ICM. The most frequently involved contrasts in confirmed HSR were iodixanol and iohexol, and iopromida was the best tolerated. Out of a total of 125 DPT, we obtained 26 positive results with only two systemic reactions (mild).
Conclusion: In most of the patients in our sample, allergy to ICM was ruled out, and in allergic patients, tolerance to an alternative ICM was established. Our protocol is safe and allows patients to receive ICM in the future.

Introduction

Iodinated contrast media (ICM) are essential tools in modern radiology. Thanks to new formulations with lower toxicity, their use have increased with more than 75 million administrations worldwide each year. As a result of its widespread use, adverse effects are common.[1]

Hypersensitivity reactions (HSRs) to ICM can be immediated (< 1 hour) or delayed (> 1 hour). Recent studies have shown that the overall incidence of confirmed HSRs to ICM

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ranges from 0.15% to 0.69%, with severe reactions occurring in 0.005-0.013% cases. Despite this low incidence, the potential for severe reactions necessitates careful patient evaluation and management. Additionally, the recurrence rates of HSRs are higher in patients with a history of ICM allergy, particularly among those who experience severe initial reactions.[2]

Allergy assessment using skin and provocation tests is a vital step in the management of patients with HSR to ICM. These tests allow for accurate diagnosis, safe alternatives identification, prevention of severe reactions, and avoidance of unnecessary premedication guidelines.

The aim of our study was to find out the real incidence of allergy to ICM among patients referred for suspected allergy; also described are the population characteristics, type of reactions, and the main ICM involved. The accuracy of our diagnostic protocol was demonstrated.

Material and Methods

An observational, descriptive, and retrospective epidemiological study was conducted, including patients referred from January 1, 2020, to December 31, 2022, to the Allergy Unit of the University Hospital of Fuenlabrada for suspected allergy to ICM. All patients signed informed consent. This study protocol was reviewed and approved by the Ethics Committee for Research on Medicinal Products of the University Hospital of Fuenlabrada, approval number (Comité d'Éthique de la Recherche) CEIm 22/109. After an exhaustive clinical history, we selected the protocol to be followed according to the type of reaction (Figure 1).

Severity of the reaction was established according to Brown's classification. Skin tests included skin prick test with undiluted ICM, and if negative, intradermal test with 1/10 dilution. For the basophil activation test (BAT), we tested ICM in two concentrations—0.3 mg/mL and 3 mg/mL We considered positive for the stimulation index (SI) at >2.

According to international literature, drug provocation test (DPT) with ICM should be performed in case of mild reaction to the negative skin tests. Alternative ICM should be selected for DPT in case of severe reaction or positive skin tests with the ICM or others. For delayed reactions, ICM should be administered in two separate sessions.[3,4]

Results

A total of 108 patients were analyzed. Of these, 65.7% of the patients were female, with a mean age of 58.7 years, and 24% patients had an atopy history. Regarding the characteristics of the initial reaction, immediate reactions occurred most frequently in 56 patients (52%). Delayed reactions were reported by 49 patients (45.4%) and 3 patients could not remember any type of reaction (2.8%).

The time interval between adverse reaction and allergological evaluation was more than 1 year in 44 patients (44.7%); the remaining patients were evaluated within the first year after the reaction. Allergy was confirmed in 29 patients (26.9%), assuming that in 9 patients (8.3%), a diagnosis of allergy by anamnesis was due to a severe HSR. All patients tolerated DPT with an alternative ICM. A total of 14 intradermal tests were positive for ICM immediate allergic reactions while all skin prick tests were negative. BAT was performed in two patients with positive results, with three of the five ICM tested in one of them. With regard to the patch tests performed, four were positive.

After skin tests, all patients underwent a DPT with intravenous ICM. Out of the 125 DPT, we obtained 26 positive results, of which 80% (21 patients) were for the initially implicated ICM. Most of the patients (24) presented

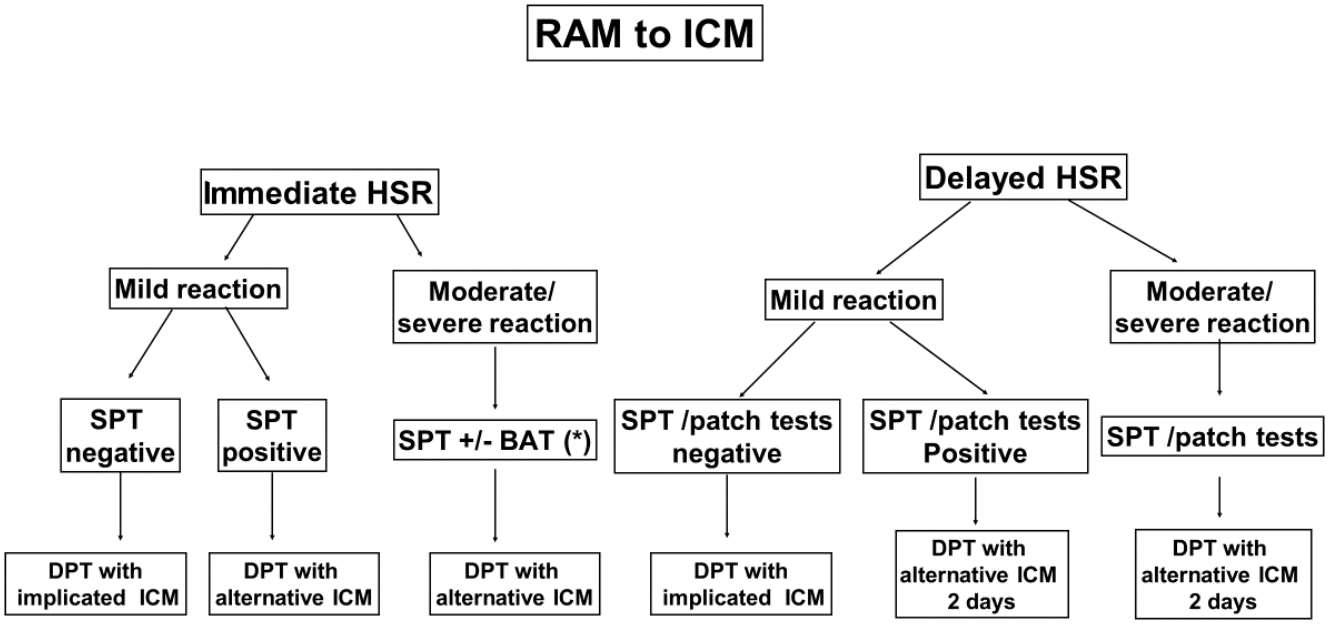

Figure 1 Study protocol for patients with suspected allergy to ICM. (*) SPT with implicated and alternatives ICM. BAT if severe reactions.

mild cutaneous symptoms (five patients with iopramide, six with iohexol, and five with iodixanol), of which only eight were delayed cutaneous reactions (three patients with iopramide and five with iodixanol). We reported only two systemic reactions, and neither required adrenaline administration (one patient suffered from hives, malaise, and sweating with iopramide and the other from urticaria and vomiting with iodixanol). Regarding the ICM used in our center (iomeprol, iobitridol, iodixanol, iohexol, and iopramide), the most allergenic involved in the reactions were iodixanol and iohexol. However, this could change due to the fact that in nearly 40% of cases, MCI involved in the reaction was unknown. Importantly, all patients with confirmed allergy tolerated an alternative ICM—the safest being iobitridol.

Discussion

This retrospective study reports a single-center experience on 108 patients with suspected allergy to MCI who underwent an allergological workup.

In previous studies with a similar sample size, MCI allergy was confirmed in a very wide range of patients (8.8–48.4%) referred for evaluation,[3,4] but in our study, allergy was confirmed in 26.9% cases.

Regarding skin test, the low incidence of positive results confirms the findings of previous studies published by Shijvers et al.[5] and Sesé et al.[6] These results could be explained by the fact that most of the immediate reactions are produced by non-immunoglobulin E (non-IgE)-mediated mechanisms and the low sensitivity of skin tests when performed 6 months after the reaction.[7.] In our study, only 46.3% of patients were evaluated in the first 2–6 months after the reaction. Taking into account the above, DPT has been recognized as the gold standard to establish the diagnosis of ICM allergy, assess tolerance, and find a safe alternative ICM.

In our study, allergy was confirmed in 29 patients (26.9%), while diagnosis was assumed in 9 others (8.3%). These patients finally tolerated DPT with an alternative ICM. These results are consistent with Meucci et al., who reported that 95.9% of the 98 patients tolerated a DPT with either the ICM or an alternative one. Regarding ICM, iodixanol and iohexol (group A) were the most frequently implicated in HSRs, likely due to their frequent use in our area. Previous publications have shown that for patients with a previous immediate HSR of any severity, using an alternative ICM without a common carbamoyl side chain can reduce recurrent HSRs during subsequent exposures.[9] Our study confirmed that iopromide (group C) was the best tolerated ICM. Considering both—the chemical differences and clinical studies results— iobitridol (group B) appears be a good choice when selecting an alternative ICM empirically.[10] In our study, all patients who underwent DPT with iobitridol tolerated it well.

Conclusions

Recommendations for patients with a history of HSR to ICM have evolved in recent years. In patients with suspected allergy to MCI, a prior allergy evaluation is essential to prevent recurrent HSRs. Although DPT is considered the gold standard for the drug allergy diagnosis, it carries potential risks of severe adverse events. However, we have demonstrated that our protocol, based on skin tests and DPT with implicated or alternative ICM, is safe and allows patients to receive ICM in the future when necessary.

Author Contributions

All authors contributed equally to this article.

Conflicts of Interest

All authors declare that they have not conflict of interest.

Competing Interests

The authors had no relevant financial or nonfinancial interests to disclose.

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References

1. Rosado Ingelmo A, Doña Diaz I, Cabañas Moreno R, Moya Quesada MC, García-Avilés C, García Nuñez I, et al. Clinical practice guidelines for diagnosis and management of hypersensitivity reactions to contrast media. J Investig Allergol Clin Immunol 2016; 26(3): 144-55. https://doi.org/10.18176/jiaci.0058
2. Vega, F., van de Ven, A.A.J.M., van der Molen, A.J. Cross-reactivity in hypersensitivity reactions to contrast agents: new classification and guide for clinical practice. Eur Radiol. 2024;34:7583–88. https://doi.org/10.1007/s00330-024-10872-8
3. Salas M, Gomez F, Fernandez TD, Dona I, Aranda A, Ariza A, et al. Diagnosis of immediate hypersensitivity reactions to radiocontrast media. Allergy. 2013;68(9):1203–6. https://doi.org/10.1111/all.12214
4. Torres MJ, Gomez F, Dona I, Rosado A, Mayorga C, Garcia I, et al. Diagnostic evaluation of patients with nonimmediate cutaneous hypersensitivity reactions to iodinated contrast media. Allergy. 2012;67(7):929–35. https://doi.org/10.1111/j.1398-9995.2012.02840.x
5. Schrijvers R, Breynaert C, Ahmedali Y, Bourrain JL, Demoly P, Chiriac AM. Skin testing for suspected iodinated contrast media hypersensitivity. J Allergy Clin Immunol,Pract. 2018;6(4):1246–54. https://doi.org/10.1016/j.jaip.2017.10.040
6. Sesé L, Gaouar H, Autegarden J-E, Alari A, Amsler E, A Vial-Dupuy, et al. Immediate hypersensitivity to iodinated contrast media: Diagnostic accuracy of skin tests and intravenous provocation test with low dose. Clin Exp Allergy. 2016;46(3):472–78. https://doi.org/10.1111/cea.12703
7. Brockow K, Romano A, Aberer W, Bircher AJ, Barbaud A, Bonadonna P, et al. Skin testing in patients with hypersensitivity reactions to iodinated contrast media – a European multicenter study. Allergy 2009;64(2):234-41. https://doi.org/10.1111/j.1398-9995.2008.01832.x

8. Meucci, E, Radice, A, Fassio, F, Sibilio, M, Iorno, M.L.C, Testi, S, et al. Diagnostic approach to hypersensitivity reactions to iodinated contrast media: A single-center experience on 98 patients. Eur Ann Allergy Clin Immunol. 2020;52(5):220-29. https://doi.org/10.23822/EurAnnACI.1764-1489.129
9. Kim S, Jeon KN, Jung JW, Park HK, Lee W, Lee J, et al. Substitution with low osmolar iodinated contrast agent to minimize recurrent immediate hypersensitivity reaction. Radiology. 2023;309(1). https://doi.org/10.1148/radiol.222467
10. Gracia-Bara MT, Moreno E, Laffond E, Muñoz-Bellido F, Lázaro M, Macías E, et al.Tolerability of iobitridol in patients with non-immediate hypersensitivity reactions to iodinated contrast media. Allergy. 2019;74(1):195-7. https://doi.org/10.1111/all.13603