ADVERSE EFFECTS OF IODINATED CONTRAST USED IN IMAGING EXAMS: CHALLENGES FOR RADIOLOGIC TECHNOLOGISTS

EFEITOS ADVERSOS DO CONTRASTE IODADO USADO NOS EXAMES DE IMAGEM: DESAFIOS PARA OS PROFISSIONAIS DAS TÉCNICAS RADIOLÓGICAS

EFECTOS ADVERSOS DEL CONTRASTE YODADO UTILIZADO EN LOS EXÁMENES DE IMAGEN: DESAFÍOS PARA LOS PROFESIONALES DE LAS TÉCNICAS RADIOLÓGICAS

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ABSTRACT

Iodinated contrast media are widely used in imaging examinations, contributing to improved image quality and increased diagnostic accuracy. However, their administration may be associated with adverse reactions of varying severity, ranging from mild manifestations such as nausea and pruritus to severe events such as anaphylaxis and contrast-induced nephropathy. This study aimed to review aspects related to the use of these agents, with emphasis on risk factors, types of adverse reactions, and prevention strategies. This is a literature review based on scientific publications and national and international guidelines. The main preventive measures include detailed medical history assessment, appropriate selection of the contrast agent, intravenous hydration in at-risk patients, and prophylactic premedication when indicated, aiming to reduce complications and improve the safety of radiological procedures.

Keywords: Contrast Media. Adverse Effects. Radiology. Patient Safety. Premedication.

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RESUMO
Os meios de contraste iodados são amplamente utilizados em exames de imagem, contribuindo para melhorar a qualidade das imagens e aumentar a precisão diagnóstica. Contudo, sua administração pode estar associada à ocorrência de reações adversas de diferentes intensidades, variando desde manifestações leves, como náuseas e prurido, até eventos graves, como anafilaxia e nefropatia induzida por contraste. Este estudo teve como objetivo revisar aspectos relacionados ao uso desses agentes, com ênfase nos fatores de risco, tipos de reações adversas e estratégias de prevenção. Trata-se de uma revisão de literatura baseada em publicações científicas e diretrizes nacionais e internacionais. Entre as principais medidas preventivas destacam-se a anamnese detalhada, a escolha adequada do contraste, a hidratação venosa em pacientes de risco e a pré-medicação profilática quando indicada, visando reduzir complicações e aumentar a segurança dos procedimentos radiológicos.

Palavras-chave: Meios de Contraste. Efeitos Adversos. Radiologia. Segurança do Paciente. Pré-medicação.

RESUMEN
Los medios de contraste yodados son ampliamente utilizados en los exámenes de imagen, contribuyendo a mejorar la calidad de las imágenes y aumentar la precisión diagnóstica. Sin embargo, su administración puede estar asociada con la aparición de reacciones adversas de diversa intensidad, que van desde manifestaciones leves, como náuseas y prurito, hasta eventos graves, como anafilaxia y nefropatía inducida por contraste. Este estudio tuvo como objetivo revisar aspectos relacionados con el uso de estos agentes, con énfasis en los factores de riesgo, los tipos de reacciones adversas y las estrategias de prevención. Se trata de una revisión de la literatura basada en publicaciones científicas y directrices nacionales e internacionales. Entre las principales medidas preventivas se destacan la anamnesis detallada, la selección adecuada del contraste, la hidratación intravenosa en pacientes de riesgo y la premedicación profiláctica cuando está indicada, con el objetivo de reducir complicaciones y aumentar la seguridad de los procedimientos radiológicos.

Palabras clave: Medios de Contraste. Efectos Adversos. Radiología. Seguridad del Paciente. Premedicación.

1 INTRODUCTION

Radiology is dedicated to the study of the organs and structures of the human body through the use of ionizing radiation, sound waves, or magnetic fields, enabling diagnoses and treatments (DE BARROS *et al*., 2025). In this context, the use of drugs in radiological examinations becomes fundamental, especially contrast media, which allow the visualization of internal structures that cannot be identified by conventional X-rays (DA ROCHA *et al*., 2024). Medium-opacity structures, such as the kidneys, heart, brain, and blood vessels, require the use of a contrast agent, with iodinated contrast agent being the most used, although it may have associated risks (MARCELINO *et al*., 2024). Contrast contributes to increasing the definition of radiographic images, providing greater diagnostic accuracy, in addition to allowing a better evaluation (SPADAFORA *et al*., 2021).

Iodinated contrast agents are used in various exams, such as urography, urethrography, arthrography, angiography, myelography, computed tomography, and interventional procedures (BERGLUND *et al*., 2024). From a chemical point of view, they have a benzene ring bonded to three iodine atoms and are classified as ionic, which dissociate into charged particles, and non-ionic, which remain stable in solution (AUGUSTO *et al*., 2020).

Despite their wide use, iodinated contrast agents can cause adverse reactions ranging from mild manifestations to more severe events (MARCELINO *et al*., 2024). In this context, the integrated performance of professionals in radiological techniques and other members of the multidisciplinary team is essential to promote the appropriate use of these agents, preventing possible drug interactions and reducing associated risks, especially in patients who use potentially nephrotoxic drugs (DA ROCHA *et al*., 2024). In addition, these professionals contribute to the definition of selection criteria, establishment of image acquisition protocols, administration and monitoring of contrast media, ensuring greater patient safety (DE SÁ *et al*., 2021).

Thus, the present review addresses the main adverse effects related to the use of iodinated contrast agents, highlighting the importance of technical-scientific knowledge and multidisciplinary action to ensure more accurate diagnoses and safety in radiological procedures.

2 METHODOLOGY

This is a literature review in the PubMed, SciELO and Google Scholar databases, using the keywords "Iodinated contrast medium", "radiological contrast" and "adverse reactions to iodine", alone or in combination. Publications from 2020 to 2025 were included,

with the exception of older studies considered relevant. All identified titles and abstracts were analyzed and selected, while studies on magnetic resonance imaging and nuclear medicine were excluded, ensuring a focus on the pertinent areas of iodinated contrast agents in general radiology and computed tomography.

3 LITERATURE REVIEW

Idinated contrast agents are indispensable tools in modern diagnostic radiology, used in examinations such as computed tomography, angiography, urography and cholangiography. Its main function is to increase the contrast between different tissues and anatomical structures, improving the quality of images and favoring more accurate diagnoses (ALVES *et al*., 2020). However, the use of these agents requires attention to possible adverse reactions, which can range from mild manifestations to severe anaphylaxis (AUGUSTO *et al*., 2020; DUTRA *et al*., 2020).

These reactions are classified as mild, moderate, or severe, and may include pruritus, nausea, urticaria, vomiting, dyspnea, bronchospasm, glottis edema, hypotension, and anaphylaxis (CÁSSIO *et al*., 2023). The most common pathophysiological mechanisms involve non-IgE-mediated hypersensitivity, osmotic changes, and activation of mast cells and endothelial cells, with consequent release of histamine and inflammatory cytokines (DE SÁ *et al*., 2021). In addition, contrast-induced nephropathy represents a relevant complication, resulting from direct tubular toxicity and reduced renal blood flow (SEELIGER *et al*., 2020).

Prior evaluation of the patient is the essential step to reduce risks, and should consider a history of allergies, kidney function, comorbidities, and use of nephrotoxic drugs (MAGALHÃES *et al*., 2024). International protocols recommend continuous monitoring during and after the examination, in addition to preventive measures, such as the administration of corticosteroids and antihistamines in patients at increased risk (RODRIGUES *et al*., 2023; BRAZILIAN COLLEGE OF RADIOLOGY AND DIAGNOSTIC IMAGING, 2024).

The chemical properties of iodinated contrast agents, especially the presence of iodine atoms, determine their ability to absorb radiation and enhance structures in exams (DUTRA *et al*., 2024). Ionic contrasts, with higher osmolality, are associated with a higher incidence of adverse effects, while non-ionic contrasts, with lower osmolality and more controlled viscosity, are safer and better tolerated, being preferred in vulnerable patients (DE SÁ *et al*., 2021; CÁSSIO *et al*., 2023).

The incidence of adverse reactions varies according to the type of contrast agent and the population profile. Studies indicate rates between 0.1% and 13%, with ionic contrasts

accounting for the highest occurrences (3% to 12%), while non-ionic contrasts are less frequent (0.2% to 3%) (MARCELINO *et al*., 2024). Most cases are mild, accounting for more than 80% of reactions, whereas severe manifestations such as bronchospasm, angioedema, hypotension, and anaphylaxis are less common (0.02% to 0.6%). Approximately 70% of events arise in the first five minutes after administration, which justifies the need for immediate observation and emergency support (SOLÉ *et al*., 2021). Delayed reactions, such as skin rash and fever, are self-limiting but may reappear in individuals with a prior history of sensitivity (CHIU *et al*., 2022).

Iodinated contrast agents are indispensable inputs to clinical practice and diagnostic radiology, providing detailed visualization of vessels, cavities, and parenchymal structures. Mastery of its physicochemical properties, indications, and risks is essential to ensure safety, efficacy, and diagnostic quality in radiological procedures (SPADAFORA *et al*., 2021; CIRAQUE *et al*., 2022).

3.1 IODINATED CONTRAST: CHEMICAL PROPERTIES AND APPLICATIONS

Iodinated contrast agents represent a fundamental class of pharmacological substances used in modern diagnostic radiology. Its main function is to increase the differentiation between tissues and anatomical structures, allowing greater sharpness and detail in the images obtained by exams such as computed tomography, angiography, and urography (CÁSSIO *et al*., 2023). The use of these compounds has revolutionized radiological practice, providing earlier and more accurate diagnoses, in addition to assisting in the therapeutic planning and follow-up of various pathologies (SPADAFORA *et al*., 2021)

Chemically, iodinated contrast agents are classified into two broad groups**:** ionic and nonionic. Ionic agents dissociate into charged particles in solution, with high osmolality, usually four to eight times higher than that of blood plasma (CÁSSIO *et al*., 2023). This characteristic is directly associated with a higher risk of adverse effects, such as allergic reactions, feelings of discomfort during injection, local pain, hemodynamic changes, and even electrolyte disturbances (DUTRA *et al*., 2020). Due to these limitations, their use has been gradually replaced by non-ionic agents (BRAZILIAN COLLEGE OF RADIOLOGY AND DIAGNOSTIC IMAGING, 2024).

Nonionic contrasts, on the other hand, keep their molecular structure intact and exhibit low osmolality, which significantly reduces the incidence of adverse reactions and improves patient tolerability. Because they are safer, they are preferentially used in vulnerable populations, such as the elderly, neonates, pregnant women, and individuals with a history of hypersensitivity to iodinated contrast agents (CÁSSIO *et al*., 2023). This category also has

a viscosity that is more suitable for intravenous administration, allowing greater comfort and less risk of vascular irritation (DA ROCHA *et al.*, 2024).

In addition to osmolality, viscosity is a physicochemical property that determines the performance of these agents. More viscous substances tend to flow less easily through catheters and blood vessels, which can make injection difficult and compromise the homogeneity of the enhancement. For this reason, it is often recommended to preheat the contrast to temperatures close to body temperature, which reduces its viscosity and improves its distribution in the body (BRAZILIAN COLLEGE OF RADIOLOGY AND DIAGNOSTIC IMAGING, 2024).

A detailed understanding of these chemical and physical properties is critical for safe patient management and proper contrast agent selection. The choice of type and dose should consider factors such as the individual's clinical condition, renal function, the type of test to be performed, and the route of administration (ZENG *et al.*, 2024). Such care is essential to prevent complications, among which contrast-induced nephropathy due to tubular toxicity, renal hemodynamic alterations, and hypersensitivity reactions mediated or not by immunological mechanisms stand out (DA ROCHA *et al.*, 2024).

Transient phenomena, such as a feeling of heat, facial flushing, and metallic taste, are relatively common and usually self-limiting. These effects result, in large part, from plasma expansion and contrast interaction with the vascular endothelium, promoting local histamine release and activation of non-immunoglobulin-mediated pathways (AUGUSTO *et al.*, 2020). Although benign, these symptoms reinforce the importance of continuous observation of the patient during the examination and the availability of immediate pharmacological and professional support (CHIU *et al.*, 2022).

Therefore, mastery of the physicochemical and biological mechanisms of iodinated contrast agents is indispensable for the safe practice of diagnostic radiology. Technical knowledge allows professionals involved in radiological procedures, especially professionals in radiological techniques, to select the appropriate agent and adjust administration protocols. This integrated action contributes directly to the reduction of risks, the optimization of diagnostic results, and the strengthening of patient safety in the radiological environment.

3.2 MECHANISMS OF ACTION OF IODINATED CONTRAST AGENTS

The mechanisms of action of iodinated contrast agents underlie their diagnostic applicability in radiology. Iodine, the main chemical element of these agents, has a high atomic number and high X-ray absorption capacity, which increases attenuation in the structures where it is distributed, generating differential enhancement between tissues and

greater anatomical definition in the images (RODITI *et al*., 2022). After administration, the contrasts are rapidly distributed throughout the vascular compartment and diffuse into the interstitial space, according to the blood flow of the tissues, evidencing highly vascularized organs, such as the kidneys, liver, and brain. The intravenous route is the most used, especially in emergency and highly complex protocols (BRAZILIAN COLLEGE OF RADIOLOGY AND DIAGNOSTIC IMAGING, 2024).

At the molecular level, contrast acts by physically interfering with the transmission of X-rays, without metabolic involvement. Iodine absorbs photons due to its electron density, generating radiographic contrast proportional to tissue concentration, which facilitates the identification of lesions, tumors, and ischemia (BONTRAGER, 2022). Its excretion occurs almost entirely through the renal route within 24 hours, without metabolization, requiring caution in patients with compromised renal function, due to the risk of induced nephropathy (CIRAQUE *et al*., 2022).

The osmotic effect constitutes another relevant mechanism: high-osmolality contrasts can cause hemodilution, vasodilation, and transient discomfort, while low- or iso-osmolality formulations reduce these adverse effects (DUTRA *et al*., 2020). In addition, interactions with endothelial membranes can increase vascular permeability in inflamed areas, favoring the diagnosis of infectious processes, but can also induce hypersensitivity reactions mediated by histamine and bradykinin in predisposed individuals (JUNIOR, 2025).

In summary, iodinated contrast agents act by physical and chemical mechanisms based on the interaction of iodine with ionizing radiation, ensuring diagnostic accuracy and clinical safety (SANTOS, 2025).

3.3 TYPES AND RISK FACTORS OF ADVERSE REACTIONS TO IODINATED CONTRAST AGENTS

Adverse reactions to iodinated contrast media are classified according to the time of onset and pathophysiological mechanism into immediate and late reactions, and may be toxic, immunological (allergic) or non-immunological (BONTRAGER, 2022). The most frequent immediate reactions occur up to one hour after administration and range from mild, such as itching and urticaria, to severe, such as intense bronchospasm, anaphylactic shock, and cardiovascular collapse (AUGUSTO *et al*., 2020). The incidence ranges between 0.1% and 0.7% with nonionic agents (ZENG *et al*., 2024). Late reactions, on the other hand, manifest between one hour and ten days, with predominantly cutaneous, self-limited and mild symptoms (MARCELINO *et al*., 2024; BRAZILIAN COLLEGE OF RADIOLOGY AND DIAGNOSTIC IMAGING, 2024).

In the pathophysiological field, toxic reactions are related to the physicochemical properties of the contrast, and can cause induced nephropathy, arrhythmias, and transient vasodilation (RIBEIRO *et al*., 2023). Immunological hypersensitivity reactions may involve IgE, while non-immunological reactions result from direct complement activation and release of inflammatory mediators (MARCELINO *et al*., 2024).

Among the risk factors, a previous history of adverse reaction, allergic diseases, asthma, COPD, renal failure, diabetes mellitus, and concomitant use of metformin stand out (AMERICAN COLLEGE OF RADIOLOGY, 2024; SILVA *et al*., 2022). Extreme age and general weakness also increase susceptibility (CÁSSIO *et al*., 2023).

Detailed prior evaluation, including clinical history and renal function, associated with preventive protocols and continuous monitoring, is essential to reduce adverse events and ensure diagnostic safety (DA ROCHA *et al*., 2024).

3.4 PREVENTION AND MANAGEMENT OF ADVERSE REACTIONS

The prevention and management of adverse reactions associated with iodinated contrast agents are essential to ensure patient safety in radiological practice (DA ROCHA *et al*., 2024). The identification of individuals at higher risk requires a detailed anamnesis, considering factors such as previous history of contrast reactions, presence of allergies, atopic diseases, renal dysfunction, cardiovascular diseases, and use of medications (BRAZILIAN COLLEGE OF RADIOLOGY AND DIAGNOSTIC IMAGING, 2024).

Among the main preventive strategies, the preference for the use of non-ionic and low-osmolality contrast agents stands out, which have a lower incidence of adverse reactions. In addition, in cases where the glomerular filtration rate is less than 30 mL/min/1.73m², hydration should be performed according to the evaluation and recommendation of the attending physician, considering the clinical conditions and individual risk factors of each patient. According to the guidelines of the Brazilian College of Radiology and Diagnostic Imaging, intravenous hydration is one of the main preventive measures to reduce the risk of kidney injury associated with the use of iodinated contrast media. One of the recommended protocols is the administration of 0.9% saline solution (0.9% NaCl) at a dose of 1 mL/kg/hour, starting approximately 3 to 4 hours before the administration of contrast medium and remaining for 4 to 6 hours after the procedure. This strategy aims to promote adequate renal perfusion, increase urinary flow, and reduce the concentration of contrast in the renal tubules, contributing to minimize potential nephrotoxic effects and increase patient safety during radiological procedures (BRAZILIAN COLLEGE OF RADIOLOGY AND DIAGNOSTIC IMAGING, 2024).

In selected patients, especially those with a history of previous reactions to contrast, at the discretion of the physician, intravenous (IV) and/or oral (OP) prophylactic premedication may be considered, with the use of corticosteroids associated with antihistamines, with the aim of reducing the frequency and severity of hypersensitivity reactions (AMERICAN COLLEGE OF RADIOLOGY, 2024). For services that adopt this strategy, a combination of a corticosteroid and an antihistamine administered prior to the test is recommended.

The Brazilian Association of Allergy and Immunology recommends the use of premedication regimens with corticosteroids and antihistamines for patients at risk of reaction to iodinated contrast, with variations according to age and clinical condition (ASBAI, 2016).

- Prednisone 50mg, PO, 13 hours, 7 hours, 1 hour before the exam with iodinated contrast or prednisolone 32mg, PO, 12 hours and 2 hours before the exam with iodinated contrast E
- Fexofenadine 180mg, PO, 1 hour before the iodinated contrast agent or diphenhydramine 50mg, PO, 1 hour before the iodinated contrast exam (ASBAI, 2016; ASCIA, 2022).

In cases where the individual cannot receive the oral medication, administer hydrocortisone IV 200mg, 4-6 hours before the exam with iodinated contrast, and diphenhydramine 50mg IV, 1 hour before the exam with iodinated contrast (ASBAI, 2016; ASCIA, 2022).

For pediatric use, it is suggested:

- Prednisone or prednisolone 0.5 to 0.7 mg/kg/dose (up to 40 mg/dose), PO, 13 hours, 7 hours, and 1 hour before the exam with iodinated contrast E
- Fexofenadine suspension 6 mg/mL: up to 15 kg – 5 mL; 15 to 25 kg – 7.5 mL; over 25 kg – 10 mL 1 hour before the exam with iodinated contrast OR desloratadine 2mL (children 6 months to 2 years), 2.5mL (children 2 to 6 years) and 5mL (children 6 to 12 years) 1 hour before the exam with iodinated contrast, PO OR diphenhydramine, 1.25 mg/kg, PO, 1 hour before the exam with iodinated contrast (maximum 50mg) (ASBAI, 2016).

In patients admitted to the emergency room, who need to perform an imaging exam quickly or patients with a request for an imaging exam, the indication in adults is:

Methylprednisolone 40mg IV or hydrocortisone 200mg, 4-6 hours before the exam with iodinated contrast and diphenhydramine 50mg IV, 1 hour before the exam with iodinated contrast. (ASBAI, 2016; ASCIA, 2022).

In cases of allergy to methylprednisolone or hydrocortisone, administer dexamethasone 7.5 mg IV or betamethasone 6 mg IV, 4 to 6 hours before the use of contrast, in addition to diphenhydramine, 50 mg IV, 1 hour before the examination with iodinated contrast (ASBAI, 201).

However, in situations where the test needs to be performed immediately, use only diphenhydramine, 50mg IV, because corticosteroids are not effective when used in a period of less than 4-6 hours before contrast. It is worth remembering that diphenhydramine cannot be done in hypotensive patients (ASBAI, 201).

In pediatrics, use methylprednisolone 2 mg/kg IV, before the procedure with iodinated contrast agents together with diphenhydramine, 1 to 2 mg/kg, up to 50 mg, IV (ASBAI, 201).

Tables 1, 2 and 3 present a simplified application proposal, based on the literature discussed, to be used according to medical evaluation, and is indicated for patients with a history of non-severe reactions or with increased risk. It is noteworthy that such an approach does not completely eliminate the risk, requiring continuous clinical surveillance and the availability of an emergency kit.

Table 1

Premedication schedule

Medicinal product	Adult Dosage	Period before the iodinated contrast exam
Prednisolone	*32mg, PO**(5, 20.40mg)	12 h and 2 h before
Fexofenadine	180mg PO	1h before

Note: PO = oral route. *According to medical advice, dose adjustment may be necessary depending on the patient's clinical conditions, possible drug interactions or the commercial availability of the drug. **The wording mentioned refers to commercial availability at the time of the study.
SOURCE: Elaborated by the author.

Table 2

Alternative premedication regimen

Medicinal product	Adult Dosage	Period before the iodinated contrast exam
Prednisone	*50mg PO**(5 and 20 mg)	1 pm, 7 am and 1 hour before
Diphenhydramine	50 mg PO	1h before

Note: PO = oral route. *As directed by the doctor, dose adjustment may be necessary depending on the patient's clinical conditions, possible drug interactions or the commercial availability of the drug. **The formulation mentioned refers to the commercial availability at the time of the study. Contraindicated in hypotensive patients.
SOURCE: Elaborated by the author.

Table 3

Pediatric premedication regimen

Medicinal product	Pediatric Dosage	Period before the iodinated contrast exam
Prednisolone	0.5–0.7 mg/kg PO (maximum dose: 40 mg)	1 pm, 7 am and 1 hour before
Fexofenadine	PO suspension (6 mg/mL) : up to 15 kg – 5 mL; 15 to 25 kg – 7.5 mL; over 25 kg – 10 mL	1h before

Note: PO = oral route.
SOURCE: Elaborated by the author.

The patient should be continuously monitored during contrast administration, as about 70% of adverse reactions occur within the first few minutes, with the availability of emergency drugs and advanced life support (EUROPEAN SOCIETY OF UROGENITAL RADIOLOGY, 2022). Mild reactions require contrast interruption and symptomatic therapy, while moderate or severe cases require adrenaline, ventilatory and hemodynamic support, and in some cases intensive care unit support (ARAI *et al*., 2021). The notification of adverse events contributes to pharmacovigilance and review of protocols in health institutions (BRAZILIAN COLLEGE OF RADIOLOGY AND DIAGNOSTIC IMAGING, 2024).

4 FINAL CONSIDERATIONS

Iodinated contrast agents play an essential role in diagnostic radiology, contributing significantly to the improvement of image quality and diagnostic accuracy. However, despite their benefits, the use of these agents is not without risks, and may cause adverse reactions ranging from mild manifestations to severe events, such as anaphylaxis and contrast-induced nephropathy.

The prevention and management of these reactions depend on well-defined institutional protocols, careful clinical evaluation by the multidisciplinary team, with adequate risk stratification, patient monitoring, and adoption of preventive measures, such as adequate hydration, appropriate choice of the type of contrast agent and, when indicated, the use of prophylactic premedication.

In this context, the integrated performance of the multiprofessional team, associated with the implementation of evidence-based clinical protocols and the use of monitoring technologies, contributes to the reduction of risks and better patient safety. Finally, the need for continuous scientific updating and strengthening of institutional protocols is emphasized, aiming at safe practice and excellence in contrast-enhanced radiological procedures.

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