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Multidisciplinary Clinical Protocol of Management of Hypersensitivity* Reactions to Contrast Media in Radiology

Protocolo Clínico Multidisciplinar de Abordagem das Reações Agudas de Hipersensibilidade a Meios de Contraste em Imagiologia

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Abstract

Acute hypersensitivity reactions to contrast media(AHRC) are infrequent, usually mild but potentially fatal. Although there are recommendations from Radiology, Intensive Care and Allergology fields regarding its management, a clinical multidisciplinary protocol that integrates these complementary approaches is missing.
We aimed to elaborate a protocol that includes adverse reactions definition and classification; identification of risk factors and management of patients with AHRC.
A non systematic revision of national and international guidelines was made regarding the management of hypersensitivity reactions, in order to elaborate a clinical consensus protocol to be used in different medical fields (Radiology, Allergology and Intensive Care).
Non-renal adverse contrast reactions can be classified in chemotoxic (related to contrast chemical properties) and hypersensitivity reactions (with involvement of immunological mediators IgE and non IgE mediated); and in mild, moderate and severe (regarding severity), with different therapeutic approaches. Identified risk factors are previous contrast media reaction and asthma. Pre-medication decreases the probability of symptoms but does not exclude the possibility of a severe reaction. Patients suspected of AHRC should be observed in an allergy clinic to confirm the diagnosis and find an alternative contrast media. Clinical alert record as well as the notification of reaction to surveillance system of adverse drug reactions should be performed.
This clinical expert's protocol consensus based on national and international guidelines aims to be a valuable practical tool in the management of patients that need contrast media during a radiologic exam.

Keywords

Contrast media; Hypersensitivity; Adverse reaction; Radiology.

Resumo

As reações agudas de hipersensibilidade a meios de contraste (RAHC) em imagiologia são consideradas pouco frequentes; são habitualmente ligeiras, mas podem ser potencialmente fatais. Apesar de existirem recomendações nacionais e internacionais sobre a sua abordagem, não existe um protocolo clínico que integre a visão de todas as especialidades envolvidas (Imagiologia, Imunoalergologia e Medicina Intensiva).
Pretendeu-se estabelecer um protocolo prático de utilização transversal e adequada à realidade hospitalar, que inclua a definição das reações adversas e sua classificação, a identificação de factores de risco para a ocorrência de reação de hipersensibilidade, a abordagem diagnóstica e terapêutica e de orientação dos doentes com RAHC.
Realizou-se uma revisão não sistemática das recomendações nacionais e internacionais acerca da abordagem das RAHC, publicadas pelas sociedades científicas de Imagiologia, Imunoalergologia e Medicina Intensiva e o protocolo foi elaborado por consenso de peritos destas especialidades.
As reações adversas não renais subdividem-se em reações quimiotóxicas (relacionadas com as características de cada contraste) e reações de hipersensibilidade (com envolvimento de mediadores imunológicos de forma IgE e não IgE mediada); podem ser classificadas em ligeiras, moderadas e graves com abordagens terapêuticas específicas. Constituem os principais factores de risco para a sua ocorrência, a reação prévia a meio de contraste e a asma brônquica. A pré-medicação diminui a probabilidade de ocorrência de sintomas, mas não exclui a possibilidade de reação grave. Os doentes com suspeita de reação de hipersensibilidade devem ser encaminhados para a consulta de Imunoalergologia para diagnóstico definitivo, orientação para redução de risco e escolha de meio de contraste alternativo. A inserção de alertas clínicos, assim como a notificação deve ser assegurada.
Este protocolo clínico de consenso de peritos, baseado nas indicações nacionais e internacionais atuais, pretende ser uma ferramenta passível de utilização na prática clínica aquando da abordagem do paciente a realizar exames imagiológicos que necessitem de meio de contraste.

Palavras-chave

Meios de contraste; Hipersensibilidade; Reação adversa; Imagiologia.

*Authors' note: In this document, and following the SEAIC designation proposal[7], acute non-renal adverse reactions, allergic and allergic-like, are referred to as acute contrast media hypersensitivity reactions in imaging.

1. Objectives

- To adress the definition of acute hypersensitivity reaction to contrast media and the differential diagnosis with chemotoxic reactions;
- To determine risk factors for acute hypersensitivity reactions;
- To establish laboratory procedures to be performed in case of suspected allergic reaction;
- To standardize criteria for clinical diagnosis and treatment of acute hypersensitivity reactions; and
- To define orientation criteria for the allergology appointment.

Delayed adverse reactions (from one hour to several days after administration of contrast media) and nephrotoxic reactions are outside the scope of this protocol.
This protocol should be applied to all patients undergoing a radiologic study with administration of contrast media as part of the best practices associated with the use of contrast media in any radiology department.
Various contrast media and various routes of administration are used in imaging; by the frequency and clinical significance of associated acute adverse reactions, this protocol refers only to iodinated contrast media and gadolinium-based ones when administered intravenously or intra-arterially.

2. Definitions

An acute non-nefrotoxic adverse reaction to a contrast media is a noxious and unintentional reaction that occurs up to one hour after the administration of the contrast media and does not result from the nephrotoxic effect.
These reactions can be observed with iodinated contrast media in procedures such as Angiography, Urography and Computed Tomography and with gadolinium contrast agents in Magnetic Resonance Imaging being, however, more frequent with iodinated contrast media. In terms of severity, the majority of reactions are mild, whereas life-threatening situations are rare.
Acute non-nephrotoxic adverse reactions may be subdivided into chemotoxic reactions and hypersensitivity reactions.

Chemotoxic reactions:

- are related to the chemical properties of the contrasts administered, and generally depend on the dose and on the infusion rate;
- are usually transient and self limited, but can be serious. They frequently include heat sensation, flushing, nausea and vomiting;
- vagal vase reactions are a less frequent type of chemotoxic reactions characterized by hypotension and bradycardia;
- cardiovascular adverse effects should also be considered in the context of chemotoxic reactions, such as arrhythmias, cardiac contractility depression, hypertensive crisis and cardiogenic pulmonary edema. In cases of severe hypotension, loss of consciousness, cardiorespiratory arrest, angina, or seizure may occur. These effects are very rare;
- the occurrence of these reactions does not prevent the administration of contrast media in future imaging studies.

Hypersensitivity reactions:

- are idiosyncratic and unpredictable, and may occur in response to administration of minimal amounts of contrast media
- can be allergic, mediated by IgE / T lymphocytes or allergic-like mediated by non-specific mechanisms of release of vasoactive mediators (direct endothelial membrane effect, complement system activation or direct formation of bradykinins).

3. Classification of adverse reactions according to severity

The AHRC classification can be made according to clinical severity, in mild, moderate and severe reactions (Table 1).
In cases of severe cardiovascular reactions, such as pulmonary edema, significant hemodynamic instability and cardio-respiratory arrest, although these reactions may result from a chemotoxic reaction, an allergic etiology may be assumed for future treatment and referral of the patient, especially if signs and symptoms of skin and mucosa involvement coexist.

Table 1 - Classification of adverse reactions according to severity

Hypersensitivity reactions	Chemotoxic reactions
Mild	
Limited urticaria / pruritus Limited skin edema Scratched throat Nasal congestion Sneezing / conjunctivitis / rhinorrhea	Limited vomiting and nausea "Flushing" / heat sensation Transient tremors Headache / dizziness Anxiety Taste alteration
Moderate	
Generalized urticaria / pruritus Diffuse erythema with stable vital signs Facial edema without dyspnea Wheezing / slight bronchospasm	Vomiting and severe nausea Hypertensive urgency Isolated chest pain Vasovagal reaction (which requires treatment and responds to treatment)
Severe	
Facial or generalized edema with dyspnea Diffuse erythema with hypotension Laryngeal edema with stridor and/or hypoxia Wheezing / bronchospasm with hypoxia Non-cardiogenic pulmonary edema Anaphylactic shock	Resistant vasovagal reaction Arrhythmias Convulsions Hypertensive emergency Cardiogenic pulmonary edema

4. Classification of contrast media

Iodinated contrast media (ICM) are iodine salts whose chemical structure includes a benzene ring with at least 3 iodine atoms which is responsible for the radio-opacity.
The ICM can be classified according to iodine molecule loading (ionic and nonionic), molecular structure (monomeric and dimeric) and osmolarity (hyperosmolar, low osmolarity and iso-osmolarity). Contrast osmolarity is the most frequently associated factor with hypersensitivity

reactions and reactions are more frequent with those with high osmolarity.
Most ICM are classified as:

- monomeric ionic - have the highest osmolarity, are essentially used in extravascular procedures such as cystograms;
- dimeric ions - the only example is ioxaglate and is low in osmolarity;
- monomeric nonionic - are considered second generation, have low osmolarity - examples: iohexol, iopamidol, ioversol, iopromide, ioxylan, iomeprol;
- dimeric non-ionic - example: iodixanol - is associated with equal or lesser number of hypersensitivity reactions than those of low osmolarity.

The contrast media used in magnetic resonance are gadolinium complexes that can be classified as ionic or nonionic and according to their structure in linear or macrocyclic.

5. Prevalence

With low osmolarity ICM, the prevalence of acute hypersensitivity reactions is very low (0.2% to 0.7%) and severe reactions are even rarer (0.04%).
With gadolinium-based contrast media the prevalence of acute hypersensitivity reactions is much lower than with iodinated contrast (ranging from 0.24% to 0.07%), and severe allergic reactions are extremely rare (with prevalence of 0.01 to 0.001%).

6. Risk factors for hypersensitivity reaction

Two types of risk factors can be considered

a) Relative to the contrast media
Reactions are more frequent with high osmolarity contrast media, however the prevalence of serious reactions seems to be independent of the degree of osmolarity.

b) Regarding the patient
The main risk factors for contrast media hypersensitivity reactions are:

- Previous history of AHRC in an imaging study with contrast media administration.
- Unstable asthma

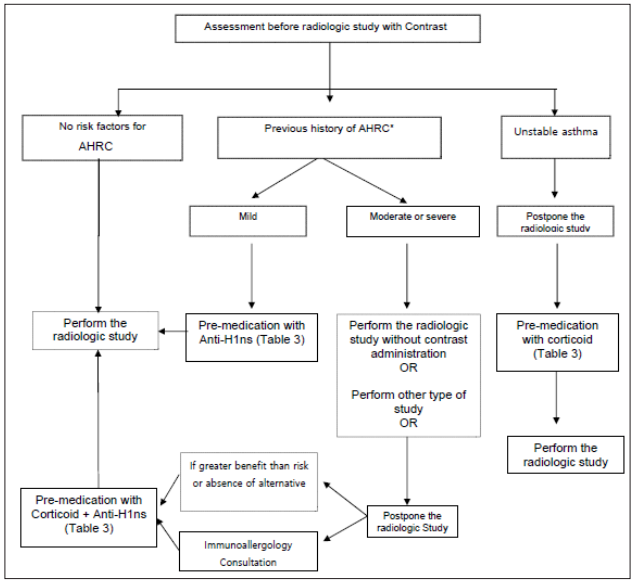
Some authors consider that previous history of bronchial asthma, drug allergy, food allergy, female gender may be a relative risk factor, however, these do not prevent the administration of contrast media nor do they determine the need for premedication.
It should be noted that the occurrence of a chemotoxic reaction in a previous exam with intravenous contrast media is not a risk factor for the occurrence of hypersensitivity reaction, therefore there is no need to pre-medicate these patients.
The approach of the patient submitted to a radiologic study with contrast media is explained in Figure 1.

7. Attitudes to be taken in patients with risk factors

a) General measures

- There should be reciprocal information and coordination between the team of technicians and nurses, and the neuro / radiologist;

Figure 1 - Approach of the patient who will be examined with contrast medium



* To ICM if a CT or angiography or urography is indicated; to gadolinium-based contrast media if a MRI is indicated.
Anti-H1 ns- antihistamine H1non sedative

- The patient should remain in the imaging service, in the area of the CT / MRI, with venous access, for 30 min;
- If you give an antihistamine with a torpor effect (eg clemastine IV) to a patient, he/she should not drive or work with machines within 6 hours or as long as the symptoms of drowsiness remain.

b) if there is a history of mild hypersensitivity reaction

- The examination must be performed;
- Intravenous contrast can be performed, if important for the diagnosis;
- If the CM to be administered is identical to that associated with previous adverse reaction, consider non-sedating antihistamine 30 minutes before the test (Tables 2 and 3)

c) If history of moderate to severe hypersensitivity reaction

- Consider performing the radiologic study without contrast media;
- Consider carrying out another type of study;
- Postpone examination and:
  - If possible, refer the patient to an allergology consult in order to carry out an allergy study and establish a diagnosis and specific guidelines;
  - According to the benefit, especially in the absence of an alternative, perform the imaging study with contrast media after "premedication" measures, according to the clinical situation - Corticoid + Anti-H1ns (Tables 2 and 3).
- In this situation, consider using another active pharmacological principle of contrast media, different from the one used in the previous study in which the hypersensitivity reaction occurred.

d) If unstable asthma
In case the patient reports medical diagnosis of asthma and presents with uncontrolled symptoms such as wheezing or bronchospasm, dyspnea and low effort tolerance:

- Consider performing the radiologic study without contrast media;

- If it is necessary to perform a radiologic study with CM administration, it must be postponed and have premedication programmed - corticoid - in this particular case it is important to perform the corticoid as an anti-edematous (Tables 2 and 3).

e) If history of allergic reaction to other allergens

Follow the general indications specified above; this situation, by itself, does not require premedication.

Table 2 - Pre-medication scheme according to risk factors

Pre-medication scheme
Previous history of mild hypersensitivity reaction to contrast Non-sedative anti-H1 2nd generation, orally (PO), 30 min before contrast administration (Table 3)
Previous history of moderate to severe hypersensitivity reaction to contrast and examination cannot be postponed waiting for allergology appointment **a) Adults and >12 year-old children** Prednisolone 50mg 13, 7 and 1 hour before PO or methylprednisolone 32mg PO 12h and 2h before PLUS Non-sedative anti-H1 2nd generation PO 2 h prior to administration of contrast media If the patient cannot take oral medication choose for i.v pre-medication: Ex: Hydrocortisone 200mg iv, 12h and 2h before contrast + Clemastine 2mg 2h prior to administration of contrast media If situations not programmed arise (patients in the ER): Ex: Hydrocortisone 200mg and every 4h / 6h, until the radiologic study + clemastine 2mg ev 1 hour before contrast. **b) ≥ 6 year-old children** Prednisolone 0.5 mg / kg PO 13, 7 and 1 h before or methylprednisolone 1 mg / kg PO 12 h and 2 h before PLUS Non-sedative anti-H1 2nd generation per os 2 h prior to administration of contrast media **c) < 6 year-old children** Ex: Betamethasone 0.03 mg / kg PO (in general it corresponds to 2 drops per kg); 12 and 2 hours prior to administration of contrast agent PLUS Non-sedative anti-H1 2nd generation PO 2 h prior to administration of contrast media
Unstable asthma **a) Adults and >12 years-old children** ex: prednisolone 0,5mg PO, 12h and 2h prior to contrast media administration. **b) ≥ 6 years-old children** ex: prednisolone 0,5mg/Kg (max 50mg), PO, 12h and 2h prior to contrast media administration. **c) < 6 years-old children** ex: betamethasone 0,03 mg/Kg PO (in general it corresponds to 2 drops per Kg); 12h and 2h prior to contrast media administration.

8. Considerations for chemotoxic reactions

In order to minimize chemotoxic reactions in contrast medium in imaging, we must:

- Administer contrast in imaging study only if there is a diagnosis benefit;
- Comply with the manufacturer's handling and packaging instructions;

Table 3 - Drugs that can be used as pre-medication

Name	Formulation	Children dose	Adults dose
Antihistamine			
Fexofenadine	S,C	6-12 year-old: 30 mg >12 year-old:120-180 mg 1x/day	120-180 mg
Cetirizine	S,C	2 - 5 year-old: 2,5 mg 6 - 11 year-old: 5 mg >12 year-old: 10 mg/ day	10 mg
Loratadine	S,C	2 - 11 anos: ≤ 30 kg: 5 mg > 30 kg: 10 mg >12 year-old, > 30 kg: 10 mg	10 mg
Levocetirizine	S,C	2 - 5 year-old: 1,25 mg 6 - 11 year-old: 5 mg > 12 year-old: 5 mg	5 mg
Desloratadine	S,C	1 - 5 year-old: 1,25 mg 6 - 11 year-old: 2,5 mg > 12 year-old: 5 mg	5 mg
Ebastine	S,C	2 - 5 year-old: 2,5 mg/ day 6 - 11 year-old: 5 mg/ day >12 year-old: 10,0 mg/ day	10-20 mg
Rupatadine	S,C	2 - 11 year-old, 10 - 25 kg: 2,5 mg ≥ 25 kg: 5,0 mg > 12 year-old: 10 mg	10 mg
Bilastine	C	> 12 year-old: 20 mg/ day	20 mg
Clemastine	IM, IV	0,025 mg/Kg	2 mg
Corticoids			
Prednisolone	C, IV	0,5 mg/Kg PO 0,5 mg/Kg IV	50 mg PO 50 mg IV
Metilprednisolone	C, IV	1 mg/Kg PO 0,5 mg/Kg IV	32 mg PO 40 mg IV
Hydrocortisone	IV	4 mg/Kg	200 mg
Betametasone	S	< 6 year-old: Betamethasone 0,03 mg/Kg PO (corresponding in general to 2 drops per Kg);	
Deflazacort	S,C	< 6 year-old 1 mg /Kg(= 1 drop per Kg)	30 mg

S-Oral solution C-pill A-years PO-orally IV-intravenous

- In the case of ICM, use iso-osmolar or low osmolarity contrast agents;
- Administer the minimum required dose/volume and the lowest flow rate possible, according to the clinical indication for the radiologic study;
- In the case of ICM, to calculate volume and flow rate, the patient's profile should also be taken into consideration, namely the presence of cardiac pathology and the risk of water overload;
- Realize that anxiety, on its own, may be responsible for the occurence of symptomatology identical to a true adverse reaction to contrast media.

9. Treatment of non-renal acute adverse reactions to contrast media

Any patient may develop, in any contrast-enhanced radiologic study, an acute adverse reaction, which should be promptly identified and treated. The patient should be guided in order to obtain a clinical or clinical-laboratory diagnosis, with implications in future radiologic studies.

The approach of acute non-renal adverse reactions to contrast media is summarized in Figure 2.

There are a number of universal measures that should be taken in all adverse reactions, including suspension of contrast administration, oxygen mask and monitoring:

- Elimination of the triggering factor is essencial, meaning in this case the interruption of contrast media infusion.
- Every patient should be placed in a comfortable position. Patients may prefer to be seated as it will ease their breathing. Dorsal decubitus, with elevation of the lower limbs, is useful in hypotensive patients and when we think a vagal reaction is occurring. If you feel that the patient is going to faint, he/she should not sit or stand up. The patient should be placed where he can easily take off the clothes in order to observe the progression of skin lesions.
- Monitoring should always include at least respiratory rate, pulse oximetry, noninvasive blood pressure, and heart rate.
- Oxygen must be placed by facial mask (high concentration mask) until the clinical situation is reevaluated.

In the event of a mild reaction, only the universal measures should be taken and if the symptoms are resolved, the patient's surveillance must be kept in the radiology department for at least 30 minutes after the resolution of the symptoms.

If the suspicion is mild hypersensitivity reaction, a second generation non-sedative antihistamine drug may be used.

In the event of a moderate or severe reaction, the Medical Emergency Team (MET) must be immediately activated. If a hypersensitivity reaction is suspected, the on duty imaging physician should immediately administer Adrenalin IM (see Table 4). Until the arrival of the MET, the professionals present must take the Basic Life Support measures appropriate to the clinical case.

9.1. Treatment of chemotoxic reactions

The treatment of these reactions is symptomatic and directed to the type of reaction.

The majority of reactions are mild; it is advisable to keep patient surveillance in the imaging department until 30 minutes after the resolution of symptoms.

If the reaction is moderate or severe, the MET should be involved to do intensive treatment. In this case the surveillance should be extended until 8 hours, in an inpatient regime.

9.2. Treatment of hypersensitivity reactions

9.2.1 Mild reactions

In the event of a mild reaction, the universal measures, monitoring and surveillance described above must be taken. The indicated antihistaminic drugs are non-sedative (Table 3) or in the case of impossibility of oral use, for example

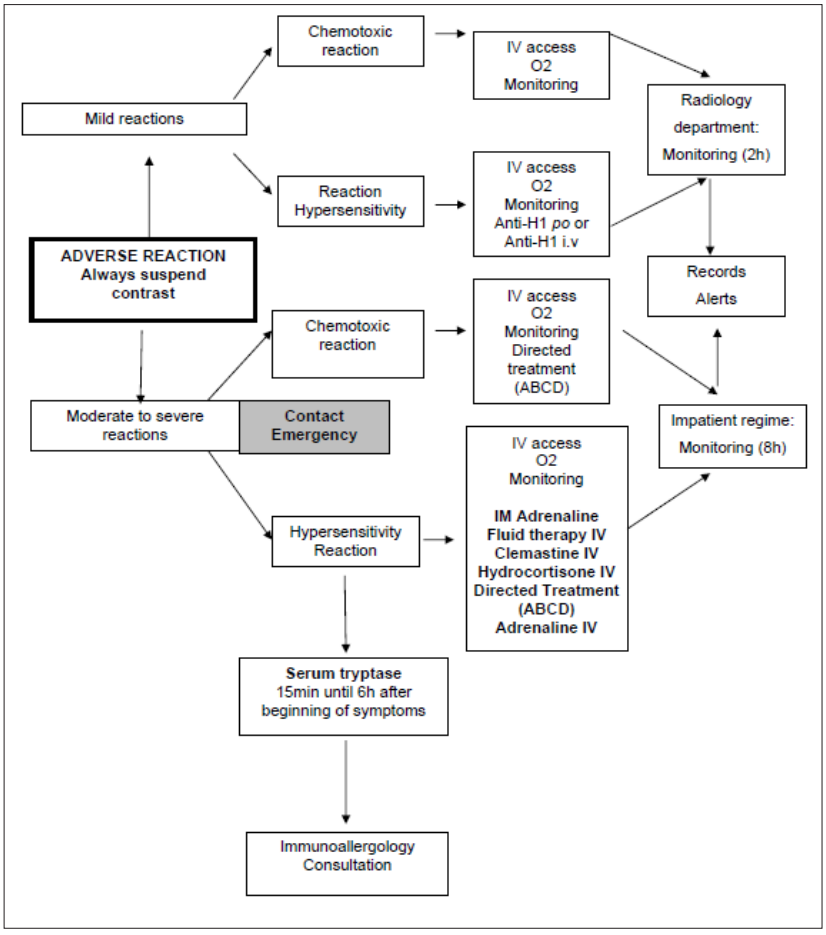


Figure 2 – Treatment of hypersensitivity reactions to contrast media

Clemastine (the adult dose is 2 mg IV or IM, in children the correct dose is 0.025 mg / kg / IM or EV dose (up to a maximum of 2 mg) may be used, see table 4.

9.2.2 Moderate or severe

A moderate or severe AHRC is likely to be present when a patient develops sudden and unexpected illness (usually within minutes after administration of contrast media), with rapidly progressing skin changes and potentially fatal airway and / or respiratory and / or circulatory system compromise. The allergic reaction, being a specific and potentially fatal type of adverse reaction, has a specific approach. This approach should be appropriate to the clinical severity of the illness. This acting algorithm is based on the recommendations of the European Resuscitation Council (ERC).

ABCDE approach

The ABCDE methodology of recognition and approach of any critical patient is the one that should be used in these situations.

Airway (A - airway) problems may correspond to edema of the airways, and may be manifested as hoarseness or stridor and may progress to complete obstruction and cardio-respiratory arrest. Airway obstruction can occur quickly. The warning signs are edema of the tongue and lips and hoarseness. Early involvement of an airway expert (experienced anesthesiologist, intensivist) is mandatory in the treatment of these patients. It is necessary to consider early tracheal intubation; any delay can make intubation extremely difficult. A surgical airway may be necessary if tracheal intubation is not possible.

Breathing problems (B - breathing) can lead to dyspnea; wheezing, whistling; cyanosis; and confusion, frequently related to the presence of bronchoconstriction and respiratory failure.

Circulatory problems (C - circulation) can range from hypotension to cardiac arrest. Circulatory problems (often referred to as anaphylactic shock) may be caused by direct myocardial depression or vasodilatation and increased capillary permeability.

Airway, Breathing, and Circulation problems referred above may alter the patient's neurologic status (D - disability) due to decreased cerebral perfusion. There may be confusion, agitation and loss of consciousness.

Adrenalin

It should be noted that if there is suspicion of moderate or severe hypersensitivity reaction, the drug of choice is Adrenalin.

There are no absolute contraindications for treatment with intramuscular adrenalin in an anaphylaxis situation. Adverse effects are very rare when the correct doses are injected intramuscularly (IM). Subcutaneous or inhalation routes are not recommended.

In adults and children over 12 years of age, administer an initial dose of 0.5 mg IM adrenalin (0.5 ml ampoule 1 mg / ml (1: 1000 adrenalin) = 0.5 mg = 500 mcg). Additional doses may be administered at intervals of about 5 min, depending on the patient's response, up to 3 administrations.

In children 6 to 12 years of age the dose of adrenalin is 0.3 mg IM (0.3 ml ampoule 1 mg / ml (1: 1000 adrenaline) = 0.3 mg = 300 mcg). In children less than 6 years of age the dose of adrenalin is 0.15 mg IM (0.15 ml ampoule 1 mg / ml (1: 1000 adrenalin) = 0.15 mg = 150 mcg) (Table 4).

Table 4 - Drugs used in the treatment of hypersensitivity reactions

ADRENALINE **(always administered IM - dose by weight - 0.01 mg / kg / dose)** **Adult and >12 year-old child** - administer an initial dose of 0.5 mg IM adrenalin (0.5 ml 1 ampoule 1 mg/ml = 0.5 mg = 500 mcg). Additional doses may be given at intervals of about 5 min up to 3 doses. **6 to 12 year-old Children** - administer an initial dose of 0.3 mg of IM adrenalin (0.3 ml of 1 ampoule of 1 mg/ml = 0.3 mg = 300 mcg). **<6 year-old Children** - administer an initial dose of 0.15 mg IM Adrenalin (0.15 ml 1 vial of 1 mg/ml = 0.15 mg = 150 mcg).
Adrenaline IV (only in case of lack of response to IM adrenaline and by a doctor with experience in its use) **(dilute one ampoule of adrenaline (1mg/ml) up to 100ml of saline solution - a concentration of 10ug / ml)** **Adult**: Bolus of 20 to 50 ug repeated every 1-2 minutes if necessary; perfusion of 0.1-1 ug / kg / min, the same dilution can be used Pediatrics: continuous infusion 0.1-1 ug / kg / min. Bolus IV not applicable.
FLUIDS **Adult** - fast fluid bolus IV (500-1000 ml crystalloid), if necessary administer additional doses. **Children** - fluid bolus IV (20 ml/kg of crystalloids).
OTHER DRUGS **Clemastine** – 0,025 mg/kg/dose EV/IM (max - 2mg) **Hydrocortisone** – adult - 200 mg; children - 4 mg /kg **Glucagon (resistance to adrenaline in beta-blocked patients)** - bolus of 30 µg/kg / IV dose up to a maximum of 1 mg (may be repeated every 5 minutes) Continuous perfusion 5-15ug/min (dilute one ampoule to 100ml of saline solution (10ug/ml))

The best place for IM injection is the anterolateral zone of the middle third of the thigh. The needle must be long enough to ensure that adrenalin is injected into the muscle (21G green color, 4 cm, also known as an intramuscular needle).

IV adrenalin should only be administered by professionals experienced in the use and titration of vasopressors in clinical practice (eg: anesthesiologists or intensivists). In patients with spontaneous circulation, intravenous adrenalin may cause potentially fatal hypertension, tachycardia, arrhythmias, and myocardial ischemia. Do not administer the 1: 1,000 IV adrenalin solution without proper dilution (dilute 1 mg to 100 ml saline, you can use this dilution for bolus or for infusion). Titrate adrenalin IV in bolus of 20 to 50 mcg (2 to 5 ml of the proposed dilution) depending on the response. In children, do not titrate Adrenalin IV in bolus. If repeated doses are required, establish IV infusion of adrenalin using the existing tables (1 to 10 mcg / min is the usual dose which corresponds to 6 to 60 ml/h of the previous dilution, titrating for the intended effect).

Adrenaline is the first-line vasopressor for the treatment of allergic reactions. Ponder other vasopressors and inotropes (noradrenaline, vasopressin, terlipressin) when the initial resuscitation with adrenalin and fluid is not successful. These drugs should only be used in specialized settings (eg: in intensive care units) where there is experience in their

use. Glucagon may be useful in treating allergic reactions in patients taking beta-blockers.

Fluid therapy
Timely fluid therapy is one of the determining factors to avoid and correct hypotension / distributive shock that may lead to cardiorespiratory arrest.
Rapid fluid bolus IV (500-1000 ml adult crystalloid) should be administered, monitoring the response and if necessary administering additional doses. In children, a bolus of crystalloid fluids of 20 ml/ kg is recommended. In this context, Crystalloid are preferable as they are isotonic and glucose-free use (such as Poly® or Plasma-Lyte®).

Other drugs
The administration of antihistamines, although reducing the symptoms is not life saving and should never delay the administration of intramuscular adrenaline. The suggested antihistamine drug is Clemastine. The adult dose is 2 mg I.V or I.M. In the child the correct dose is 0.025mg/kg/dose I.M. or E.V (up to a maximum of 2mg).
There is little evidence to support the routine use of H2 antihistamines (eg ranitidine, cimetidine) for the treatment of these conditions.
The administration of corticosteroids is mainly for the prevention of biphasic reactions (resurgence of allergic reaction after 6 to 8 h) and it is neither life saving and should never delay the administration of intramuscular adrenalin. There is little evidence as to the ideal dose of corticosteroids; for example, the hydrocortisone suggested dose in adults is 200 mg IV and in child 4 mg/kg IV slow.

Cardiorespiratory arrest
In the event of a cardio-respiratory arrest, advanced life support measures should be immediately initiated, in accordance with the latest ERC guidelines.

10. Laboratory procedures

The diagnosis of hypersensitivity reactions is clinical. There are several differential diagnoses that should be considered according to the severity of the clinical manifestations, and excluded when necessary, never delaying the treatment intervention.
In all moderate to severe AHRC, a blood sample should be taken for quantification of serum tryptase levels. When? as early as possible between 15 minutes to 6 hours after the onset of symptoms.
In all moderate to severe AHRC, an allergology appointment is required. The increase of serum triptase supports the diagnosis of IgE-mediated hypersensitivity, but, if normal, an anaphylactic reaction must not be excluded. In case of increase in the serum triptase value, a new sample should be taken after the resolution of the symptoms, during the patient's follow-up. Other complementary studies will be performed during follow-up.

11. Discharge and follow-up

Patients with moderate to severe hypersensitivity reactions should be treated and observed for at least 8 hours in a facility that is capable of treating these conditions. The exact incidence of biphasic reactions that could warrant prolonged surveillance is unknown. There is no reliable way to predict who will undergo a biphasic reaction. Thus, it is important that discharge decisions are made for each individual patient by an experienced physician. There is no indication for outpatient maintenance if all symptoms are resolved.

Before discharge, all patients should:
- Be informed about the nature of the reaction and the need to continue clinical research. The patient should also be informed that he/she should avoid the contrast media until he/she goes to the allergology appointment.
- Get clear instructions to return to the hospital if symptoms resurface.
- Be referred to a specialist in allergology.

11.1 Referral to an allergology medical appointment
The following patients should be referred to an allergology appointment:
- Patients with increased risk of contrast media hypersensitivity reaction (suspicion of moderate or severe reaction prior to contrast product). Referral by the imaging physician or the physician requesting the radiologic study.
- Patients who had a moderate or severe AHRC.

12. Records

12.1 Clinical records
Whenever an acute non-nephrotoxic adverse reaction occurs to the contrast media a clinical record should be made. This record should contain a description of the clinical manifestations, therapy performed and time elapsed until resolution of symptoms.

12.2 Pharmacovigilance registration
The adverse reaction should also be recorded on the "National Registry" (eg, INFARMED in Portugal).

13. Alerts

The insertion of the hypersensitivity reaction information into the patient's clinical / electronic process is fundamental to prevent future administrations and reactions.

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Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

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References

1. World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis, F. E. R. Simons.
2. Norma da DGS N.º 014/2012 – Anafilaxia: Abordagem Clínica.
3. Norma da DGS N.º 004/2012 – Anafilaxia: Registo e Encaminhamento.
4. ACR Manual on Contrast Media Version 10.3 2017 ACR Committee on Drugs and Contrast Media.
5. European Resuscitation Council Guidelines for Resuscitation 2015: Section 4. Cardiac arrest in special circumstances. Anatolij Truhlář et al. Resuscitation, October 2015, Pages 148 – 201.
6. ESUR Guidelines on Contrast Media, version 9.0, 2016, European Society of Urogenital Radiology.
7. Clinical Practice Guidelines for Diagnosis and Management of Hypersensitivity Reactions to Contrast Media J Investig Allergol Clin Immunol. 2016; 26:144-55.