Summary of Recommendations in English

Summary of recommendations of Hypersensitivity Reactions to CM

Module 1: Clinical question
What is the optimal treatment for acute hypersensitivity reactions after administration of contrast media?

Recommendations

Preparation:
- Have the drugs (as a minimum requirement: adrenaline, salbutamol, H1-antihistamine (clemastine) IV, and corticosteroid IV (for example prednisolone)), equipment and protocol for treatment of an acute adverse reaction readily available in every room where contrast agents are administered.
- Adhere to local protocols for accessibility of a resuscitation and emergency response team.
- Keep every patient with an acute hypersensitivity reaction to CM in a medical environment for at least 30 minutes after contrast agent injection. Moderate and severe reactions need a prolonged observation.

Acute management general principles:
- Check and stabilize patient according to the ABCDE method.
- Stop infusing contrast agent and replace IV line with crystalloid.
- Dyspnoea or stridor: let patient sit up.
- Hypotension: keep patient in prone position, raise legs.
- Consider measuring serum tryptase (see recommendations in chapter Laboratory Diagnosis of Hypersensitivity Reactions to Contrast Media).
- Record acute allergic reactions in allergy registry (see chapter Organization of Healthcare).

Note: After administration of clemastine the patient may no longer be able (or insured) to drive a car/motorcycle or to operate machinery.

Severe reactions:
Cardiac or respiratory arrest:
- Start CPR.
- Call the CPR team.

Anaphylactic reaction or stridor:
- Call rapid response team (SIT-team).
- Give oxygen 10 to 15 L/min with non-rebreathing mask.
- Give 0.5mg adrenaline IM in lateral upper thigh.
- Give fluid bolus of crystalloid 500ml IV in 10 minutes, repeat as necessary.
- Consider nebulizing with salbutamol 5mg or budesonide 2mg for stridor.
- Give clemastine 2mg IV, repeat as necessary.
- Consider adding corticosteroid (for example prednisolone 50mg IV*).

*Or equivalent dose of other corticosteroid
50 mg prednisolone is equivalent to:
- 40 mg methylprednisolone.
- 8mg dexamethasone.
- 200mg hydrocortisone.

*Consider adding corticosteroids to prevent protracted or biphasic anaphylactic reactions if initial symptoms are severe.

Moderate reactions:
Consider transferring the patient to a department with facilities for monitoring of vital functions.

Isolated bronchospasm:
- Salbutamol 2.5 to 5mg nebulization in oxygen by facemask 10 to 15 L/min (nebulization is easier to administer and more effective than dose aerosol).
- In mild cases asthma patients may use their own salbutamol dose aerosol.
- In case of deterioration give adrenaline 0.5mg IM and consider call rapid response team.

Isolated facial oedema without stridor:
- Give oxygen 10 to 15L/min via anon-rebreathing mask.
- Give clemastine 2mg IV.
- If oedema is severe or near airways or if stridor develops: treat as anaphylaxis.

Isolated urticaria/diffuse erythema:
- Give clemastine 2mg IV.
- If accompanied by hypotension: treat as anaphylaxis.

Isolated hypotension:
- Give bolus of crystalloid 500ml IV, repeat as necessary.
- If accompanied by bradycardia, consider atropine 0.5mg IV.
- If accompanied by other symptoms: treat as anaphylaxis.

Mild reactions:

General:
- Mild reactions may only need reassurance.
- Observe vital signs until symptoms resolve.
- Do not remove iv access during observation.

Consider:
- Prescribing a non-sedating antihistamine, for example desloratadine 5mg PO (once daily) for mild allergic reactions.
- Ondansetron 4mg IV for protracted vomiting.

Module 2: Clinical question
What is the optimal treatment for late hypersensitivity reactions to contrast media?

Recommendations

Warn patients who have had a previous hypersensitivity reaction to contrast media, that a late hypersensitivity reaction may be possible, usually a skin reaction.

Patients should contact their general practitioner if they have a late hypersensitivity reaction after CM administration.

Consider informing the radiology department where the CM was administered about the occurrence and symptoms of a late hypersensitivity reaction after CM administration.

When the symptoms of a late hypersensitivity reaction are mild, a wait-and-see approach can be justified.

Treat late hypersensitivity reactions symptomatically.
Consider treatment of skin reactions with oral or topical corticosteroids.

When severe symptoms develop, such as generalized pustulosis or painful cutaneous blisters, refer the patient to a dermatologist.

Module 3: Clinical question
What is the diagnostic value of laboratory testing for hypersensitivity reactions to contrast media?

Recommendations

Do not perform a Basophil Activation Test routinely in all patients with a history of hypersensitivity reactions receiving contrast medium.

Measure serum tryptase between 1 to 2 hours from the start of all moderately severe to severe acute hypersensitivity reactions to contrast media.

When tryptase is elevated, refer the patient to a drug allergy specialist.

Module 4: Clinical question
What is the diagnostic value of skin testing for hypersensitivity reactions to contrast media?

Recommendations

Do not perform skin tests routinely after every hypersensitivity reaction to a contrast medium.

Refer the patient to a specialist in drug allergy to perform skin tests within 6 months after the hypersensitivity reaction in the following patient groups:
- Severe hypersensitivity reactions to a contrast medium.
- Hypersensitivity reactions with increased tryptase levels.
- Hypersensitivity reactions to 2 or more different contrast media of the same type (for example 2 different iodine-based CM) or to 2 or more types of contrast media (for example iodine-based CM and gadolinium-based CA).

Always specify the used contrast agent in the referral.

Refer the patient to a specialist in drug allergy to perform skin tests in all patients with breakthrough hypersensitivity reactions despite premedication with corticosteroids and H1-antihistamines.

Module 5: Clinical question
Which prophylactic measures should be taken in patients with increased risk of hypersensitivity reactions after contrast administration?

Recommendations (See also Flowcharts 1 – 4)

I Patients with a previous (acute) hypersensitivity reaction to a **known ICM or GBCA**

A Elective (plannable) examinations with ICM or GBCA

In all patients with a (documented) history of a hypersensitivity reaction to an iodine-based or gadolinium-based CM, consider an alternative imaging modality. When this is not

possible, consider performing unenhanced exam, if this has an acceptable reduction in diagnostic quality.

If the previous hypersensitivity reaction was mild:
- Choose a different ICM or GBCA*.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

If the previous hypersensitivity reaction was moderate:
- Choose a different ICM or GBCA*.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

In cases of doubtful severity consider referring the patient to a drug allergy specialist for allegologic skin testing with a panel of different iodine-based or gadolinium-based CM.

If the previous hypersensitivity reaction was severe:
- If clinically reasonable, defer the imaging study until results of allergologic skin testing are available.
- Refer the patient to a drug allergy specialist for allegologic skin testing with a panel of different iodine-based or gadolinium-based CM.
- Apply the advice of the drug allergy specialist with regard to choice of alternative CM and use of premedication in future examinations.
- If no or positive advice for premedication: Premedicate with 2 x 25 mg prednisolone PO/IV** 12h and 2h before CM administration and 2mg clemastine IV within 1h before CM administration.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

B Acute (within hours) or emergency (direct) examinations with ICM or GBCA

In all patients with a (documented) history of a hypersensitivity reaction to an iodine-based CM, consider an alternative imaging modality. When this is not possible, consider performing unenhanced exam, if this has an acceptable reduction in diagnostic quality.

If the previous hypersensitivity reaction was mild:
- Choose a different ICM or GBCA*.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

If the previous hypersensitivity reaction was moderate:
- Premedicate with 50 mg prednisolone IV** and 2 mg clemastine IV within 30min before CM administration.
- Choose a different ICM or GBCA*.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

If the previous hypersensitivity reaction was severe:
- Premedicate with 50 mg prednisolone IV** and 2mg clemastine IV within 30min before CM administration

- Choose a different ICM or GBCA*.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

II Patients with a previous (acute) hypersensitivity reaction to an **unknown ICM or GBCA**

A Elective (plannable) examinations with ICM or GBCA

In all patients with a (documented) history of a hypersensitivity reaction to an iodine-based or gadolinium-based CM, consider an alternative imaging modality. When this is not possible, consider performing unenhanced exam, if this has an acceptable reduction in diagnostic quality.

If the previous hypersensitivity reaction was mild:
- Proceed with the radiologic examination normally.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

If the previous hypersensitivity reaction was moderate:
- Proceed with the radiologic examination normally.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

In cases of doubtful severity consider referring the patient to a drug allergy specialist for allergologic skin testing with a panel of different iodine-based or gadolinium-based CM.

If the previous hypersensitivity reaction was severe:
- If clinically reasonable, defer the imaging study until results of allergologic skin testing are available.
- Refer the patient to a drug allergy specialist for allergologic skin testing with a panel of different iodine-based or gadolinium-based CM.
- Apply the advice of the drug allergy specialist with regard to choice of possible CM and use of premedication in future examinations.
- If no or positive advice for premedication: Premedicate with 2 x 25 mg prednisolone PO/IV** 12h and 2h before CM administration and 2mg clemastine IV within 1h before CM administration.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

B Acute (within hours) or emergency (direct) examinations with ICM or GBCA

In all patients with a (documented) history of a hypersensitivity reaction to an iodine-based or gadolinium-based CM, consider an alternative imaging modality. When this is not possible, consider performing unenhanced exam, if this has an acceptable reduction in diagnostic quality.

If the previous hypersensitivity reaction was mild:
- Proceed with the radiologic examination normally.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

If the previous hypersensitivity reaction was moderate:

- Premedicate with 50 mg prednisolone IV** and 2mg clemastine IV within 30min before CM administration.
- Proceed with the radiologic examination normally.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

If the previous hypersensitivity reaction was severe:
- Premedicate with 50 mg prednisolone IV** and 2mg clemastine IV within 30min before CM administration.
- Proceed with the radiologic examination normally.
- Observe the patient ≥ 30 min with IV in place.
- Be vigilant to react to a possible new hypersensitivity reaction.

III Patients with previous breakthrough reactions to ICM or GBCA

In patients with breakthrough hypersensitivity reactions to iodine-based or gadolinium-based CM apply the same as above, but always refer the patient to a drug allergy specialist for allergologic skin testing with a panel of different ICM or GBCA.

IV Patients with previous hypersensitivity reactions to multiple CM

In patients with hypersensitivity reactions to multiple iodine-based or gadolinium-based CM (either 2 or more different iodine-based CM or gadolinium-based CA or to an iodine-based CM and a gadolinium-based CA) apply the same as above, but always refer the patient to a drug allergy specialist for allergologic skin testing with a panel of different ICM and GBCA.

V Patients with previous non-severe late hypersensitivity reactions to ICM or GBCA

In patients with previous mild or moderate late hypersensitivity reactions to iodine-based CM or gadolinium-based CA premedication is not recommended, even in acute or emergency examinations.

Notes:

* Consider cross-reactivity of iodine-based CM (see Introduction to this section, table 2).

**Or equivalent dose of another glucocorticosteroid
25 mg or 50 mg prednisolone is equivalent to:
- 20 mg or 40 mg methylprednisolone.
- 4 mg or 8 mg dexamethasone.
- 100 mg or 200mg hydrocortisone

Recommendations for hypersensitivity reactions after non-vascular CM administration

Small amounts of ICM or GBCA can be absorbed by mucosa and enter the systemic circulation after all types of nonvascular CM administration.

Hypersensitivity reactions after nonvascular administration of ICM and GBCA can occur, but their incidence is low to very low.

No preventive measures are indicated for ERCP or for nonvascular GBCA administration.

For other indications using ICM no firm recommendations can be given for patients that have experienced hypersensitivity reactions to CM in the past.

In patients that have experienced *severe* hypersensitivity reactions to CM in the past, alternative imaging or contrast agents should be explored with the radiologist, and a strict indication for examinations using nonvascular CM administration is needed.

In patients that have experienced *severe* hypersensitivity reactions to CM in the past, preventive measures for severe reactions as outlined in Module 5 may be followed prior to examinations using nonvascular CM administration, if possible after laboratory and skin testing by a specialist in drug allergy prior to the examination.

Summary of Recommendations for GBCA-enhanced Imaging

Module 6: Clinical Question
How can PC-AKI be prevented in administration of Gadolinium-Based (Gd) Contrast Agents (GBCA)?

Recommendations

Use optimal CM dosing based on patient weight in local dosing protocols for diagnostic MRI examinations.

Do not use prophylactic measures to avoid the development of PC-AKI in high-risk patients (eGFR<30ml/min/1.73m^2) receiving GBCA intravenously at the appropriate dose.

Do not substitute ICM with GBCA in order to avoid PC-AKI in computed tomography and/or digital subtraction angiography.

Module 7: Clinical Question
a) Which patients are at-risk for Nephrogenic Systemic Fibrosis (NSF)?
b) Which measures are necessary to prevent Nephrogenic Systemic Fibrosis?

Recommendations

Use low-risk (ionic and non-ionic) **macrocyclic** GBCAs for medical imaging in all patients. Linear GBCAs have been associated with NSF, therefore, consider **linear** agents only if a macrocyclic agents cannot answer the diagnostic question.

Make an individual risk-benefit analysis with the patient's requesting physician and nephrologist to ensure a strict indication for gadolinium-enhanced MRI using **linear** agents in patients with eGFR < 30 ml/min/1.73m^2.

For prevention of NSF in patients who are already dependent on haemodialysis or peritoneal dialysis, the administration of **macrocyclic** GBCA does not have to be followed by an immediate haemodialysis session.

To limit the amount of circulating GBCA, in hemodialysis patients the administration of **linear** GBCA should be followed immediately by a (high-flux) haemodialysis session, which is repeated on the following two days.

In predialysis patients (eGFR<15 ml/min/1.73m^2) and peritoneal dialysis patients, the risk of NSF due to **linear** GBCA should be weighed against the risk of placement of a temporary haemodialysis catheter.

Module 8: Clinical Question

What is the clinical relevance of gadolinium-based contrast agent (GBCA) induced T1w hyperintensity of the nucleus dentatus and the globus pallidus in the brain?

Recommendations

Ensure a strict indication for gadolinium-enhanced MRI and use EMA-approved GBCA in all patients to minimize possible gadolinium deposition.

Summary of recommendations for other topics

Module 9: Clinical question

How can central venous catheters (CVC), haemodialysis catheters (HC), peripherally inserted central catheters (PICC), and totally implantable venous access devices (TIVAD) be safely used for the administration of intravenous contrast agents, particularly using power injectors and higher injection rates for obtaining high-quality images?

Recommendations

Note: High quality of imaging is generally needed for low-contrast situations, such as in staging studies in brain, head & neck, hepatobiliary, genitourinary or colorectal imaging.
Lower quality may be acceptable for high-contrast situations such as in follow-up studies of lymph nodes (lymphoma, testicular cancer) or in pulmonary or musculoskeletal imaging.

Use a power injector and a peripheral venous access catheter for IV contrast media administration to obtain the best level of quality of contrast-enhanced imaging, especially in low-contrast situations (see Note).

When a peripheral venous catheter is unavailable: Check the position of the CVC, TIVAD, or PICC line and its patency before and after the power-injected contrast administration.

Power-injectable central venous catheters may be safely used for administration of CM using a power injector, when most recent recommendations of the catheter manufacturer are followed.

Power-injectable haemodialysis catheters may be safely used for administration of CM using a power injector, when most recent recommendations of the catheter manufacturer are followed.

Especially in haemodialysis patients, vein preservation should weigh heavily in the choice of access for CM administration. When the use of a peripheral vein for contrast administration in haemodialysis patients is inevitable, the veins in the elbow fold should be used as much as possible. If this is impossible, veins on the back of the hand or the use of dialysis fistula for contrast administration should be considered in consultation with a nephrologist.

There is a risk of catheter tip migration of PICCs and TIVADs when CM is injected via a power injector in patients with a catheter tip position above the tracheobronchial angle.
When a power-injectable PICC or TIVAD is used for CM administration, check the position of the catheter tip with DX, CT or fluoroscopy before and after power-injection of CM.

When a power-injectable CVC, HC, PICC or TIVAD is used for CM administration with a power injector, check the patency of the catheter after the procedure by manual flush of 20ml normal saline.
When a power-injectable HC is used for CM administration, immediately after power-injection a patient-specific lock solution should be installed by a certified dialysis nurse.

See Appendix 1 for recommendations on flow rates and injection pressures for a large number of commercially available CVCs, HCs, PICCs, and TIVADs in The Netherlands.

Module 10: Clinical question
What is the optimal treatment in contrast media extravasation?

Recommendations

Consider the following treatment options for contrast extravasation:
- Try to aspirate the extravasated contrast medium through an inserted needle.
- Mark affected area.
- Use compresses, for relieving pain at the injection site.
- Use pain killers.
- Elevate the affected extremity above the level of the heart.

Record contrast extravasation and treatment in the patient record (volume, CM concentration, area, clinical findings).

Give the patient clear instructions when to seek additional medical care:
- Any worsening of symptoms.
- Skin ulceration.
- Development of any neurologic or circulatory symptoms, including paraesthesia's.
- Give the patient a patient information leaflet.

For severe extravasation injury:
- Consult a plastic surgeon.
- Notify the referring physician.