

Avoidable Errors in Dealing With Anaphylactoid Reactions to Iodinated Contrast Media

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Abstract: Contrast reactions are much less common today than in the past. This is principally because of the current and predominant use of low and iso-osmolar contrast media compared with the prior use of high osmolality contrast media. As a result of the significantly diminished frequency, there are now fewer opportunities for physicians to recognize and appropriately treat such adverse reactions. In review of the literature combined with our own clinical and legal experience, 12 potential errors were identified and these are reviewed in detail so that they can be avoided by the physician-in-charge. Basic treatment considerations are presented along with a plan to systematize an approach to contrast reactions, simplify treatment options and plans, and schedule periodic drills.

Key Words: contrast reactions, contrast media, epinephrine

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There has been a decline in the frequency of adverse reactions to iodinated contrast media over the past 20 plus years. In large part, this is because of the transition from high-osmolality, ionic contrast media to the lower-osmolality, nonionic monomeric, and dimeric agents and following initial approval of low-osmolality contrast media by the United States Food and Drug Administration in 1987.¹ This resulted in improved patient care in terms of fewer adverse effects; however, as a result of diagnosing and treating fewer adverse reactions, radiologists, technologists, and radiology nurses have had fewer opportunities to develop and maintain these necessary skills.

Acute contrast reactions are much less common compared with the pre-1987 (pre-lower-osmolality nonionic contrast [LOCM]/iso-osmolar contrast media [IOCM]) era when frequency was approximately 5% to 12%. Today, the frequency of reactions is relatively uncommon (0.2%–0.7%) and severe reactions are even less common (0.1%–0.2%). Reactions to gadolinium agents are about ¼ to ½ as frequent as to iodinated contrast agents.^{2–5}

Unless the radiologist is well versed in the appropriate identification, diagnosis, and rapid treatment of an acute reaction, there will likely be more possibilities for suboptimal treatment and associated sequelae.

When an acute contrast reaction occurs, there is frequently insufficient time or opportunity to research the treatment and medication doses.

MATERIALS AND METHODS

In our review of the literature, our combined experience of over 60 years of dealing with and teaching about contrast reactions,

and our experience as legal consultants, a number of avoidable errors have been identified. Our purpose in highlighting these errors is to educate the physician regarding specific actions that should be avoided and specific actions that should be considered in dealing with iodinated and other contrast media. The obvious goal is to improve patient care in the radiology department.

Findings

Twelve significant errors that should be avoided include:

1. Failure to prepare in advance for a possible contrast reaction.
2. Failure to get adequate pre-examination clinical assessment.
3. Failure to check the patient as soon as possible if there is a question of a contrast reaction.
4. Failure to recognize a contrast reaction.
5. Failure to know how to treat a contrast reaction.
6. Failure to recognize, delayed, or no excretion on the imaging study.
7. Failure to remove ionic high-osmolality iodinated contrast from areas or situations where it might be given erroneously and cause severe sequelae.
8. Failure to promptly and properly administer oxygen.
9. Incorrectly give 1.0 mg, instead of correct 0.1 mg of intravenous (IV) epinephrine as the initial treatment of an anaphylactic reaction.
10. Incorrectly give epinephrine instead of atropine as the primary treatment of hypotension with bradycardia.
11. Incorrectly give Benadryl as treatment for hypotension with tachycardia or incorrectly give Benadryl as the initial treatment of laryngeal edema.
12. Delay in giving epinephrine to a patient with severe bronchospasm who is unresponsive to a beta-agonist inhaler.

DISCUSSION

1. Failure to Prepare in Advance for a Possible Contrast Reaction

- A. It is necessary to have proper equipment in or immediately available to the rooms where a contrast reaction might occur.^{2,3} Suggested items include:

1. Medications or contrast reaction drug box.
2. Mouth-to-mask breather.
3. Know how to call a code from a particular room.
4. Know where the code cart is located.
5. Code Cart:

- a. Automated external defibrillators or regular defibrillator.
- b. Oxygen, including tubing and a mask.
- c. Suction, blood pressure cuff, stethoscope.
- d. Pulse oximeter.
- e. IV fluids, IV sets/tubing.

- B. It is helpful to have an outline of medication doses for specific reactions and/or a flow chart outlining the treatment plans for

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various contrast reactions posted in each room where a contrast reaction might occur.

- C. The supervising radiologist should know where the Contrast Reaction Medication Box or medications are located in each room where a contrast reaction might occur.
- D. One should be familiar with the contents of the Contrast Reaction Medication Box, particularly those drugs used to deal with the primary types of contrast reactions. These medications include the following:

Epinephrine

1:1000 concentration

1:10,000 dilution/concentration (see below)

Atropine

Beta-agonist inhaler

Nitroglycerine

Benadryl®

Corticosteroids (delayed effect)

- E. Participate in or, if not already available, set up a program of annual training in the recognition and basic treatment of adverse reactions to contrast media (See Section III for more detail).

2. Failure to Get Adequate Pre-examination Assessment

The patient should be interviewed prior to injection of contrast media.^{2,3} During the interview, the following information should be queried and considered:

- A. History of prior reaction to iodinated contrast or gadolinium agents—even with premedication, there is always the possibility of a breakthrough reaction. If this occurs, it is usually similar in severity to the prior reaction.⁶
- B. History of active asthma and/or multiple, severe allergies.^{2,3}
- C. Serum creatinine and/or estimated glomerular filtration rate.^{2,3}
- D. Medications, eg, metformin.⁶

3. Failure to Check the Patient as Soon as Possible if There is a Question of a Contrast Reaction

The radiologist must be sufficiently proximate to the patient receiving contrast so that he/she can quickly get to the patient if alerted to a potential problem, that is, the physician should not delay in personally checking the patient in such cases.² The radiologist should not rely on other less-experienced or inexperienced personnel to make decisions about whether a contrast reaction is occurring and the assessment of its severity and should get to the patient as soon as possible.

In addition to the important clinical evaluation described below, the radiologist should make certain that the patient, indeed, received contrast media and should be aware of any relevant medical history.

4. Failure to Recognize a Contrast Reaction

The radiologist should not disregard the call for assistance based upon verbiage (correct or incorrect), eg, “the patient is not feeling well.”^{2,3} Assessment can only be properly obtained by the physician after direct evaluation of the patient. The patient’s stated or related symptoms should not be disregarded or discounted prior to a proper assessment (see later). A change in the voice with increased hoarseness is a sign of laryngeal edema and should be understood as an early sign of laryngeal edema. Therefore, the physician should not:

- A. Fail to evaluate pulse rate and blood pressure of the patient.
- B. Fail to listen to patient’s lungs for wheezing.
- C. Fail to evaluate appearance of eyelids, lips, tongue, skin.

- D. Fail to evaluate the mental state of the patient.

5. Failure to Know How to Treat a Contrast Reaction

- A. Fail to know the location of medications or the code cart.^{2,3}
- B. Fail to know how to secure extra help or fail to have established an effective procedure for securing help.
- C. Fail to know the basic medications and their correct doses to treat the most common contrast reactions: (see further discussion under Numbers 9–12).

6. Failure to Recognize, Delayed, or no Excretion on the Imaging Study

Such real or apparent abnormalities of excretion can occur in the following circumstances³:

- A. Hypotension in association with a contrast reaction.
- B. Renal insufficiency.
- C. Contrast not injected or extravasated during injection.

7. Failure to Remove Ionic, High-Osmolality Contrast Media (HOCM) From Areas or Situations Where it Might be Erroneously Given and Cause Severe Sequelae

Ionic, high-osmolality iodinated contrast given intrathecally can potentially cause ascending paralysis, a serious and possibly fatal reaction.⁷ This mistake can occur when a bottle of ionic HOCM is mistaken for an intended bottle of approved LOCM and injected intrathecally in situations such as disc injections or spinal needle placement confirmation. The bottles of HOCM should be removed from any room in which this mistake could potentially occur. Additionally, considering the current lowered cost of LOCM and the current increased cost of HOCM, it can be argued that similar looking bottles of HOCM should be removed from the department to preclude such disastrous mistakes from occurring.

8. Failure to Promptly and Properly Administer Oxygen

The use of oxygen during the treatment of all contrast reactions is very important.^{2,3} Progressive hypoxia and hypoxemia can lead to a serious “downward spiral” of the patient’s condition. Hypoxia/hypoxemia can make administered drugs, used in the treatment of a reaction, less effective and, therefore, may affect the ability to reverse the patient’s reaction.

Oxygen is more effective by a mask system than by nasal prongs. Administration can be accomplished by simple mask, partial rebreather mask, or a non-rebreather mask and administration by mask is preferred unless vomiting is an issue.

When administering oxygen by mask, high flow rates are necessary to avoid carbon dioxide build up in the mask. Therefore, with a simple mask, a flow rate of 10 L/min is recommended. With a partial or nonrebreather mask, the flow rate should be 15 L/min and the bag should be filled/inflated.

The use of pulse oximetry is advised to show that adequate oxygenation is occurring.

If the patient does not have spontaneous respirations, ventilation of the patient should be started with a mouth-to-mask or bag-valve-mask. Oral airway and jaw-lift maneuver facilitate aeration. Tracheal intubation should be attempted only by those with experience and expertise; excessive loss of adequate ventilation of the patient can occur during failed attempts by inexperienced personnel. Bag-valve-mask ventilation is very effective and is recommended for radiology personnel responding to the situation of respiratory arrest.

9. Incorrectly Give 1.0 mg, Instead of Recommended 0.1 mg, IV Epinephrine as the Initial Treatment of an Anaphylactic Reaction

It is very important to know the correct dose and route of epinephrine administration, as this may vary with the type and severity of contrast reaction as well as the patient's blood pressure. The initial dose of epinephrine is^{2,3,8–10}:

Subcutaneous: 0.1 to 0.3 mg (0.1–0.3 mL) of 1:1000 concentration.

Intramuscular (IM): 0.3 mg (0.3 mL) of 1:1000 concentration.

EpiPen: (0.3 mg of 1:1000 concentration).

Intravenous: 0.1 mg (1.0 mL) of 1:10,000 dilution.

10. Incorrectly Give Epinephrine as the Primary Treatment of Hypotension With Bradycardia

The correct initial treatment of hypotension with bradycardia may include the following but does not include epinephrine^{2,3,8}:

- A. IV Fluids: normal saline, Lactated Ringer's solution.
- B. Elevate legs 70 degrees or use Trendelenburg position.
- C. Oxygen.
- D. Atropine, if fluids and leg elevation/Trendelenburg position are not effective.

Atropine (not epinephrine) is the drug of choice.

Atropine corrects the vagal stimulation that is interrupting the A-V conduction system of the heart.

A larger dose is necessary (eg, 0.6–1.0 mg) to avoid possible paradoxical bradycardic effect of small dose.

11. Incorrectly Give Benadryl as the Treatment for Hypotension With Tachycardia or Incorrectly Give Benadryl as the Initial Treatment for Laryngeal Edema

Benadryl has no place in the initial treatment of an acute systemic contrast reaction, as it may cause hypotension and may thicken airway secretions, further compromising an already narrowed airway.^{2,3,10}

During teaching sessions, Board examinations, and evaluation of US radiologists' by the authors, a commonly observed error is the "use" of Benadryl for such reactions as laryngeal edema, bronchospasm, and hypotension. This should be avoided. In the setting of laryngeal edema, it may thicken secretions.

Antihistamines do not reverse existing airway edema that occurs in the setting of an acute contrast reaction.

12. Delay in Giving Epinephrine to a Patient With Severe Bronchospasm Who is Unresponsive to a Beta-Agonist Inhaler

Progressive bronchospasm, not responding to an inhaled beta-agonist drug (eg, via a metered-dose inhaler), can progress to status asthmaticus. Epinephrine provides beta-agonist effect and should be given to the patient with accelerating bronchospasm. Delay may lead to an irreversible situation.^{2,3,10}

AN IMPORTANT CONSIDERATION: RESPONSIBILITY OF THE RADIOLOGIST AND RADIOLOGY PERSONNEL

Question: Is it reasonable to believe that the radiologist can and will provide a prompt and effective response to an infrequent although potentially life-threatening event without interval training and practice?

Answer: No.^{8,9}

The reality is that patients reasonably expect that you will provide quality care and a prompt and effective response if they should develop an adverse reaction to contrast.

Bartlett and Bynevelt⁸ have concluded, "Radiologist and trainee knowledge of immediate life-threatening contrast reaction management is deficient. Severe contrast reactions are uncommon with today's use of nonionic contrast, but they still occur. Experience in the management of anaphylaxis can only come from regular, compulsory training."

Lightfoot et al,⁹ after reviewing the results of a survey of radiologists, concluded, "Radiologists' knowledge of epinephrine for the management of severe contrast material-induced allergic reactions is deficient."

Personal Observations

We believe that many practicing radiologists could and should significantly improve their ability to prepare for and properly treat contrast reactions.

HOW TO MAXIMIZE YOUR READINESS AND RESPONSE

What Can Be Done?

Develop an action plan to:

1. Systemize an approach in dealing with contrast reactions.
2. Simplify treatment options and plans.
3. Schedule periodic "drills."

1. Systematize your approach in dealing with reactions.
 - A. Respond immediately to the possibility of a contract reaction.
 - B. Go to the patient and do not interrogate the messenger.
 - C. Calm, reassuring introduction of yourself to the patient.
 - D. Request for vital signs as soon as possible, concurrent with determining the presenting signs and symptoms.
 - E. "Hands on" assessment: pulse, voice, breathing, edema, urticaria, skin color, facial edema.
 - F. Minimize time to diagnose and treat.
2. Simplify your treatment plan.

Understand limited reaction possibilities^{2,3}:

- A. Hypotension related.
 - with tachycardia
 - Oxygen
 - Leg elevation (approximately 70 degree)
 - IV fluids (normal saline or Ringer's Lactate)
 - Epinephrine
 - with bradycardia
 - Oxygen
 - Leg elevation (approximately 70 degree)
 - IV fluids (normal saline or Ringer's Lactate)
 - Atropine
- B. Edemas

Minor

- Cutaneous, single, or diffuse hives
- No treatment usually needed for a few and relatively asymptomatic hives.
- Benadryl for scattered but symptomatic hives (if no associated hypotension or airway edema).

Major

- Bronchial wall edema/bronchospasm
- Beta-2 agonist metered-dose inhaler (2–3 puffs); if ineffective, achieve beta-adrenergic effect with epinephrine
- Oxygen
- Laryngeal edema
- Epinephrine
- Oxygen

- Pulmonary edema
 - Oxygen
 - Furosemide (Lasix)
- C. Cardiac
 - Angina
 - Get help, expertise
 - Oxygen
 - Nitroglycerine (oral or topical)
 - Electrocardiogram
 - Arrhythmia and Asystole
 - Get help, expertise
 - Oxygen
 - Electrocardiogram, ideally with auto defibrillator
 - CPR and medications as indicated
- D. Hypertensive crisis
 - Get help, expertise
 - Oxygen
 - Monitor electrocardiogram, pulse oximeter, blood pressure
 - Give nitroglycerine
 - If no response, consider labetalol
- 3. Schedule periodic instruction and drills that are required and educational activities for personnel dealing with patients who may experience a contrast reaction.

Scheduled periodic instruction and drills can be integrated with annual basic life support training programs and/or can be accomplished as separate training sessions. The learning experience for the personnel can be enhanced with “hands on” exposure to equipment and drugs. Video educational materials can also be used and made available for refresher opportunities and use with new staff. In some institutions, instruction can be followed by a quiz which, particularly in the case of resident education, can be placed in the resident’s credential folder to document competence in dealing with contrast reactions.

Additional Aids

All radiologists should know how to call a “code” and/or get help as soon as possible.^{2,3}

Emergency medications should be immediately accessible, that is, very close to the reacting patient. This can be accomplished with a box containing “key medications” in the room near the examination table or scanner, particularly if the Emergency Cart is not immediately available. A Contrast Medication Box can also reduce the confusion of being confronted with the myriad of medications contained on code carts that are used for all types of emergencies. Key medications for the initial treatment of a contrast reaction include one or more of the different concentrations of epinephrine (see later), atropine, nitroglycerine, and Benadryl, corticosteroids, syringes, needles, as above.

Medication doses can be difficult to remember with the infrequent occurrence of reactions. Therefore, it is recommended that a list of medication dosages, and perhaps even a “flow chart” for the various types of reactions, is posted in all rooms in which a contrast reaction might occur.

THE ISSUE OF EPINEPHRINE

Route of Administration

Epinephrine is the drug of choice for airway edema and frequently in cases of hypotension with tachycardia.^{2–5,9,10,12} In recent years, there has been increased diversity of opinion regarding the most appropriate route of administration of epinephrine.

There are at least 3 different routes:

- Subcutaneous.
- Intramuscular.
- Intravenous.

According to the American College of Radiology’s Manual on Contrast Media, version 6.0, August 2008,³ use of epinephrine is recommended as follows:

With significant hypotension—Use IV (if no IV access use IM). Without significant hypotension, can use subcutaneous, IM, or IV routes.

For infants and small children—Use SubQ or IM (use a weight-based dose chart).

For Adults:

When given subcutaneously, the recommended dose is 0.1 to 0.3 mL (0.1–0.3 mg) of epinephrine, 1:1000 concentration.

When given intramuscularly, the recommended dose 0.3 mL (0.3 mg) of epinephrine, 1:1000 concentration.

When given intravenously, the recommended dose is 1.0 mL of epinephrine (0.1 mg), 1:10,000 dilution. This should be given slowly. Repeat as necessary to achieve response.

Intramuscular Administration

The European Society of Urogenital Radiology recommends the IM route of administration of epinephrine.¹² Their recommended dose is 0.1 to 0.3 mg IM if the patient is not hypotensive and 0.5 mg if hypotensive; and 0.5 mg IM for laryngeal edema.

Although an IM dose of 0.3 mg or 0.5 mg can be prepared by opening an ampoule of 1:1000 epinephrine, a number of institutions have made the decision to purchase a prepackaged syringe, eg, EpiPen (0.3 mg), for more expeditious access and use. This potentially saves time and decreases the possibility of a dosing error. A reminder: undiluted, 1:1000 concentration of epinephrine should not be administered intravenously because of the possibility of over dosage.

Pediatric doses should be adjusted for weight. Therefore, it is recommended that a dosage chart based on the infant/child’s weight be posted on the drug reaction “box” or on the wall in the room where contrast might be injected.

One reason for increased interest in the IM route is that many “infrequent” users of epinephrine have been confused as to: (1) when and when not to use IV epinephrine and (2) the appropriate dose to administer, particularly for IV use. Some confuse subcutaneous and IV volumes (mL) injected rather than actual dose (mg) administered.

If an error occurs, there is potential for a suboptimal outcome.

Intravenous Administration

Collins et al¹⁰ reviewed 5 years of experience with IV epinephrine used for the treatment of patients with contrast reactions during that time period. Of 456,930 patients who were given contrast, 9 had reactions that were treated with IV epinephrine. Seven of the 9 had laryngeal edema. The stated reason for IV preference is the “. . . precise control of slow IV delivery, especially if drug delivery by a nonvascular route is compromised by hypotension, peripheral vasoconstriction, or peripheral edema.” In this series, there were no deaths attributable to this medication. They do recommend caution when using IV epinephrine particularly in the treatment of patients older than 50 years and those with known coronary artery disease or systemic hypertension.

However, this cautionary comment, in our opinion has a caveat: the patient over age 50 and those with coronary artery disease who develop airway edema and hypotension need to have the airway edema reduced and the blood pressure increased so that oxygenation is improved. Epinephrine is the most effective and readily available drug to accomplish this.¹³ Otherwise, the patient with compromised vessels, low oxygen levels, and low blood pressure might very well experience cardiac and/or cerebral hypox-

emia and damage. Oxygen must get to the tissue levels. Coronary blood flow is enhanced by epinephrine or by cardiac stimulation and increased flow occurs even with doses that do not increase the aortic blood pressure.¹³ The use of very small amounts of epinephrine should not be avoided completely. Used with caution, but used correctly (ie, 1 mL [0.1 mg] of 1:10,000 dilution), a small dose of IV epinephrine administered very slowly and titrated to effect can be life saving.

SUMMARY

It is very important to understand the “basics” of preparing for, recognizing, and treating contrast reactions. Twelve common errors are highlighted and these should be avoided.

There are a limited number of severe reactions to contrast media and a limited number of primary treatment scenarios in dealing with these contrast events that need to be understood, memorized, and practiced. There are limited medications and doses that are key to proper treatment when a reaction occurs and knowledge of these is essential. Because contrast reactions occur uncommonly today, periodic review and practice is strongly recommended.

Three routes of administration of epinephrine are detailed. It is possible to use each of these routes safely, in the “proper” situation, depending upon the physician’s training, “comfort,” and expertise. Some physicians opt to use 1 route (IM) to simplify the process and minimize the chance of error. However, to not use epinephrine quickly and appropriately when it is indicated and necessary is one of the greatest errors in managing contrast reactions.

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