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Adverse Effects of Contrast Media

Incidence, Prevention and Management

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Contents

Abstract

Although contrast media are relatively well tolerated, a non–life-threatening, moderate reaction requiring some treatment occurs in 1 to 2% of patients receiving ionic high-osmolar contrast media and in 0.2 to 0.4% of patients receiving non-ionic low-osmolar contrast media. Severe, life-threatening reactions can be expected in about 0.2% of patients after injection of ionic high-osmolar and 0.04% after non-ionic low-osmolar contrast media.

Prompt recognition and treatment are invaluable in blunting an adverse response of a patient to radiographic contrast material, and may prevent a reaction from becoming severe or even life-threatening. Some reactions can be prevented by pretreatment before administration of contrast media. Knowledge, training and preparation are crucial in guaranteeing appropriate and effective therapy in the event of an adverse contrast-related event. Radiologists and their staff should review treatment protocols regularly so that each can accomplish his or her role efficiently.

The x-ray contrast media that have been used since the early 1950s are relatively well tolerated agents. However, adverse effects and reactions (table I) can be expected with an overall frequency of 7 to 54% with ionic high-osmolar contrast media and of 2 to 17% with the non-ionic low-osmolar contrast media.[1]

Adverse reactions to intravascular contrast media are generally classified as either systemic (idiosyncratic) or chemotoxic. Idiosyncratic (i.e. anaphylaxis-like, anaphylactoid) reactions occur unpredictably and independently of the dose or concentration of the agent. Most anaphylaxis-like reactions relate to release of active mediators. Conversely, chemotoxic-type effects relate to dose, the molecular toxicity of each agent and the physicochemical characteristics of the contrast agents (i.e. osmolality, viscosity, hydrophilicity, calcium-binding properties and sodium content). Some reactions to injection of contrast media (e.g. sudden cardiopulmonary arrest) are difficult to categorise specifically in either of the 2 major reaction types.[2-8]

1. Incidence

Most acute adverse reactions are minor (table II), and no treatment is required. A non–life-threatening, moderate reaction requiring some treatment occurs in 1 to 2% of patients receiving ionic high-osmolar contrast media and in 0.2 to 0.4% of patients receiving non-ionic low-osmolar contrast media.[1-8] Severe, life-threatening reactions can be expected in about 0.2% of patients after injection of ionic high-osmolar and 0.04% after non-ionic low-osmolar contrast media.[1,9]

Reported mortality rates have varied from 1 in 13 000[10] to 1 in 169 000[9] with a commonly quoted rate around 1 in 75 000.[11] No difference between ionic high-osmolar and non-ionic low-osmolar agents has been shown.[9]

Late reactions of a systemic nature to contrast media are much more common than previously appreciated. In major studies, a ratio of 2 : 1 between late and immediate reactions have been reported.[12] The introduction of the non-ionic iso-osmolar contrast media has expanded this problem. The incidence of late adverse reactions in a Japanese study was 10.9% for the iso-osmolar dimeric contrast medium and 5.6% for the low-osmolar monomeric contrast media.[13] Most of the reactions are not serious or life-threatening, but their occurrence creates anxiety among the patients and sometimes results in unnecessary calls to a doctor on duty. Skin rash is the most frequent, but flu-like illness, parotitis, headache and nausea/vomiting/abdominal pain may also be seen.

2. Risk Factors

2.1 Age

Overall, acute adverse reactions seem to be most frequent for persons aged 20 to 50 years, less frequent for persons >50 years old, and even less frequent for persons <20 years. Reactions to contrast media may be most severe in older persons, who are unable to withstand a severe systemic reaction, especially with a cardiopulmonary reaction.

Table I. Adverse reactions of contrast media

Typical reactions to contrast media
Nausea and/or vomiting
Scattered hives to extensive urticaria without respiratory symptoms
Bronchospastic reaction, i.e. asthma-like symptoms without coexisting cutaneous or vascular manifestations
Hypotension (isolated) with normal sinus rhythm or compensatory tachycardia (compensatory tachycardia may be lacking in patients taking β-blockers)
Vagal reaction, i.e. hypotension with associated sinus bradycardia
Anaphylactoid reaction: manifested by rapidly accelerating or severe bronchospasm with asthma-like wheezing, angioedema, laryngeal oedema, and developing or profound hypotension with compensatory tachycardia (compensatory tachycardia may be lacking in patients taking β-blockers)
Other reactions in relation to contrast medium injection
Cardiovascular collapse, cardiac arrest, i.e. the patient is unconscious, unresponsive, pulseless
Seizure or convulsions
Hypertensive reaction
Rigors
Anxiety reaction

Table II. Classification of severity of reactions to contrast media

Minor	Moderate	Severe
Nausea	Faintness	Hypotensive shock
Vomiting (limited)	Vomiting (severe)	Pulmonary oedema
Urticaria (limited)	Urticaria (profound)	Respiratory arrest
Pruritus	Facial oedema	Cardiac arrest
Diaphoresis	Laryngeal oedema	Convulsions
	Bronchospasm	

2.2 Allergy and Asthma

Persons with allergic tendencies are at increased risk for an idiosyncratic reaction. If there is a history of systemic allergies to multiple substances, the relative risk of reaction to contrast media is approximately twice that for the general population. In a retrospective review of patients with a history of asthma, this relative risk was approximately 5 times greater (although their status immediately pre-contrast was not assessed).[4,14]

2.3 Medications

There is debate as to whether persons taking β-blockers have an increased risk of anaphylactoid reactions. In one study,[15] anaphylactoid reactions were not statistically more frequent when the patient was taking cardioselective β-blockers, nonselective β-blockers or calcium antagonists. Patients taking calcium antagonists, which prevent immunoglobulin (Ig) E-mediator release from lung tissue, did not have a reduced prevalence of bronchospastic-type reactions. Conversely, in another study[14] there was a statistically significant increase in the frequency of anaphylactoid reactions in patients taking β-blockers, even ophthalmic preparations. Both groups noted that response to treatment for contrast reactions was sluggish or refractory in patients taking β-blockers.

There seems to be no direct correlation or association between allergy to povidone-iodine skin cleansing solution and the predisposition to an allergy-like reaction to intravascular contrast media.[7] The former is considered a type of contact dermatitis, the latter an idiosyncratic reaction.

Of interest is the increased prevalence of 'recall' reactions after administration of contrast media to patients receiving interleukin-2, a potent stimulant of the human immune system.[16,17] The reactions responded promptly to supportive therapy. Interleukin-2 recall reactions occurred less often with non-ionic contrast media; waiting more than 4 weeks between interleukin-2 treatment and the follow-up intravenous contrast medium administration also reduced reaction prevalence.[18] Different reactions, resembling hypersensitivity reactions to contrast media, occurred in patients who received intra-arterial ionic contrast media followed by intra-arterial infusions of interleukin-2.[19]

2.4 Total Dose of Contrast Media

The total dose of contrast media probably affects the prevalence of chemotoxic type reactions but will have little influence on idiosyncratic reactions. This may account for the disparity in the literature about whether the occurrence of clinically significant adverse reactions is related to the dose.[4]

2.5 Prior Reaction to Contrast Media

The prevalence of adverse reactions to conventional ionic high-osmolar contrast media in patients who have had a previous reaction to an ionic high-osmolar contrast medium, but who have not received pretreatment with corticosteroids, is 17 to 35%[20,21] or 3 to 8 times, perhaps even 11 times, greater than the risk for the general population. Administration of lower-osmolality, non-ionic contrast media to such patients reduces the frequency of repeated reactions to 5%[22,23] and new reactions are seldom more severe than the previous reaction.

2.6 Contrast Medium Nephrotoxicity

The kidney differs from the rest of the body in that the contrast agents are concentrated in the nephrons and collecting tubules. From an iodine concentration of a few mg/ml in the proximal tubules, the iodine concentration may reach several hundred mg/ml (0.1 to 0.5 M) in the collecting tu-

bules.[24] Because of their osmotic properties, the low-osmolar media will concentrate more than twice as much as the high-osmolar contrast media will. These very high-molar concentrations, especially if the patient is dehydrated, mandate that non-ionic low-osmolar contrast media and especially the non-ionic iso-osmolar contrast media should have low chemotoxicity. Whether the mechanisms for contrast medium nephropathy involve an indirect (through the vascular bed) or a direct effect (chemotoxicity) remains to be further elucidated. It is probably a combined mechanism.

The true incidence cannot be established with certainty because the incidence figures reported in different studies vary depending on the population studied and the definition of acute renal dysfunction used. Furthermore, systematic monitoring of renal function after contrast administration is not done routinely. If it is done, rarely is it done for 5 consecutive days.

Pre-existing renal impairment (serum creatinine level of >132 μmol/L) seems to be the most compelling risk factor, followed closely by factors like moderate albuminuria, hypertension, age >60 years, dehydration, uric acid (level >8.0 mg/dl) and multiple contrast studies.[25] Other risk factors include severe congestive heart failure, reduced effective arterial volume (as occurs in nephrosis and cirrhosis), multiple myeloma and administration of a high dose of contrast agent.

Concomitant use of certain drugs may also increase the risk: drugs that impair renal responses such as ACE inhibitors, aminoglycosides, for example, gentamicin, cancer chemotherapeutic agents such as cisplatin, and nonsteroidal anti-inflammatory drugs (NSAIDs). Because many patients have more than 1 risk factor, determining the independent contribution of each factor to the development of renal failure is not possible. It is generally accepted that coexistence of several or many of the factors increases the risk of contrast medium nephrotoxicity considerably. For example a patient with diabetic nephropathy has at least 3 risk factors: reduced renal function, albuminuria and hypertension. In such patients, the average incidence of contrast medium nephrotoxicity is between 15 and 25%, but may reach 90%.[9,26] In patients with other renal diseases the average incidence is 5%. In patients with no history or signs/symptoms of renal disease, the risk of contrast-induced alteration in renal function is below 1%. The incidence of acute nephrotoxicity in high-risk patients, especially patients with diabetic nephropathy, is significantly less with non-ionic low-osmolar contrast media compared with the conventional, higher osmolality ionic contrast media.[27,28] Inadequate information is available for ionic low-osmolar and non-ionic iso-osmolar contrast media; there are no obvious indications that they are more nephrotoxic than the non-ionic low-osmolar contrast media.

3. Prevention

3.1 Chemotoxic Effects

Chemotoxic effects of contrast media are more likely in patients who are debilitated or medically unstable. Hence, patients should be screened for conditions such as renal dysfunction, renovascular disease, severe cardiovascular disease or recent seizures. Alternative diagnostic procedures that do not require contrast media should be considered.

3.2 Anaphylactoid Reactions

Pretesting (intravascular, cutaneous) of patients to detect those who have an increased likelihood of having an anaphylaxis-like reaction to contrast media has been abandoned because it is insensitive and potentially dangerous.[28-30]

Patients who have asthma or multiple systemic allergies should receive lower-osmolality, non-ionic contrast media, if one is still allowed to choose between high-osmolar and low-osmolar contrast media for intravascular use (in some countries, the intravascular use of ionic high-osmolar contrast media has been banned[1]). If a patient had a mild prior reaction, the use of a non-ionic low-osmolar contrast medium without additional premedication is considered sufficient if the patient does not have other risk factors.[23,31,32] If a patient has had a previous moderate reaction to a conven-

tional, ionic contrast medium, it is recommended pretreatment be instituted with corticosteroids and antihistamines and that a non-ionic low-osmolar contrast medium be used.[32-37] However, to some extent this is reminiscent of the time when only ionic high-osmolar contrast media were used. For those same patients, other radiologists just give a non-ionic contrast medium without any pretreatment. If the patient previously had a mild or moderate reaction to a non-ionic low-osmolar contrast medium, one could also consider switching to another type of agent (e.g. iohexol instead of iopamidol or vice versa), in addition to a pretreatment regimen.

3.3 Pretreatment Regimens

Kelly et al.[32] found that by using prednisone, a corticosteroid, and diphenhydramine, a histamine H_1 receptor antagonist (antihistamine) as pretreatment, the prevalence of repeat reactions to conventional ionic contrast media decreased in their patients from an expected prevalence of between 17 to 35% to approximately 5%. Using this same corticosteroid-antihistamine regimen, Greenberger et al.[34] found that repeat reactions occurred with an incidence of 11%. With the addition of ephedrine sulfate to the corticosteroid regimen, the incidence of repeat reactions decreased to 5%, whereas the inclusion of cimetidine, a histamine H_2 receptor antagonist, increased the overall occurrence of repeat reactions to 14%. Of note was increased tremulousness in patients who received ephedrine; furthermore, ephedrine is inadvisable for patients with a history of hypertension or cardiovascular disease.

A further reduction in the occurrence of anaphylactoid reactions in patients who have previously reacted to contrast media was achieved when they received the corticosteroid-antihistamine pretreatment regimen and were examined using non-ionic low-osmolality contrast media.[38] A similar decrease with non-ionic low-osmolar contrast media plus corticosteroids has also been shown in a prospective randomised study.[35] It should be stressed that antihistamines alone (without corticosteroids) have not proved to be effective as a premedication regimen against moderate or severe reactions.[28]

A large prospective study[36,39] looked at the potential benefit of pretreating all patients with oral methylprednisolone 32mg given 12 and 2 hours before the administration of ionic high-osmolar contrast media. Significant reductions in the overall number of reactions and in mild reactions were noted. There was a trend, though not statistically significant, towards a reduction in the number of severe reactions, but reactions were not totally eliminated. Other authors[40] disagree that routine corticosteroid prophylaxis is advantageous. Moreover, although corticosteroid-antihistamine pretreatment appears beneficial in reducing the occurrence of anaphylactoid reactions, it has little effect on chemotoxic reactions.

When high-risk patients were premedicated with prednisone 50mg 13, 7 and 1 hour prior to injection of contrast material, 9% had an adverse reaction if they had an ionic high-osmolar contrast agent, whereas only 0.5% had an adverse reaction if they subsequently received a non-ionic low-osmolar contrast medium.[35,38]

3.4 Lactate Acidosis

The biguanide metformin is used in type 2 (non–insulin-dependent) diabetes mellitus.[41] Renal insufficiency with failure to clear metformin leads to the accumulation of metformin and the potential for fatal lactic acidosis.[42] The use of contrast media in patients receiving metformin is currently very controversial.[43,44] The potential danger of lactic acidosis exists because of accumulated metformin (i.e. from failure of renal excretion) and not from any interaction of contrast media and metformin. Patients at risk are those who may develop contrast medium–induced nephrotoxicity and renal insufficiency/failure. In Europe, it is currently advised that metformin should be stopped 48 hours before and for 48 hours subsequent to the administration of contrast media. In the US, it is now recommended that metformin should be stopped at the time of the study and not restarted for 48 hours. Renal function, e.g. by mea-

suring serum creatinine level, should be checked to ensure that renal function has remained at the pre-contrast level before metformin is resumed. Normal renal function, defined as a normal serum creatinine level, does not totally exclude the possible occurrence of lactic acidosis, but it is more frequent in patients with abnormal renal function defined as patients with abnormal serum creatinine levels.[45]

3.5 Contrast Medium Nephrotoxicity

Several measures have been recommended to prevent contrast medium–induced nephropathy. They include hydration with sodium chloride 0.9%, sodium chloride 0.45%, infusion of mannitol, infusion of arterial natriuretic factor, administration of loop diuretics, calcium antagonists, theophylline, dopamine, use of low-osmolar non-ionic contrast media instead of high-osmolar ionic contrast media, haemodialysis rapidly after contrast administration, minimisation of the volume of contrast medium, and prolongation of the interval between procedures where contrast media are used. Of all these many measures, extracellular volume expansion has repeatedly been shown to be effective and is most widely recommended.

Patients with pre-existing renal failure, independent of cause, should not undergo radiological procedures where contrast medium is administered without being hydrated.[46,27] The only exception is patients with congestive heart failure. An adequate hydration procedure includes administration of 0.1 L/h of 0.9% saline from 4 hours before the contrast medium administration to 24 hours after for patients who are not allowed to drink or eat because they will be undergoing an interventional or surgical procedure. Patients who can and may drink, should have at least the same volume: 0.5L of water or soft drinks before and 2.5L during the following 24 hours. This volume should cover perspiration and secure a diuresis of at least 1 ml/min. Furthermore, non-ionic low-osmolar contrast media should always be used.[26,27] The interval between 2 examinations where contrast media are administered should be at least 48 hours. Concomitant use of nephrotoxic drugs (e.g. gentamicin, NSAIDs) should be avoided.

Presence of multiple myeloma has, for many years, been considered a contraindication for administration of contrast media, since some patients developed anuria. This was because of dehydration. Although the administration of contrast media to myeloma patients is not totally risk- free (the incidence in this group of patients is about 1%), it may be performed if the clinical need arises and the patient is well hydrated.[47]

4. Treatment

The majority of patients with severe anaphylactoid reactions recover if they are aggressively and appropriately treated. Because 94 to 100% of severe and fatal reactions occur within 20 minutes of the contrast medium injection, most patients have reactions while they still are in the radiology department.[11] The ability to assess and treat their contrast reactions effectively is, therefore, an essential skill that the radiologist should have and must maintain through regular review. Rooms in which contrast material injections are done should have the emergency drugs to treat a reaction initially and emergency equipment should be either in that room or in an immediately accessible area.

The radiologist should remain nearby for at least the first critical 4 to 5 minutes following contrast injection and should stay in the immediate vicinity for the next 20 to 30 minutes. It is recommended that intravenous contrast injections be made through a short needle catheter assembly, which should be left in place (e.g. for 20 minutes) to ensure venous access in the event of a major reaction.

Basic response includes oxygen supplementation, initiation of intravascular physiological fluids, establishment of an adequate airway, and evaluation of blood pressure and heart rate. Talking with the patient as you check their pulse rate provides much initial information: breathing is assessed, the possibility of a vagal reaction (bradycardia) is determined, and an estimate of systolic pressure is gained (a palpable radial artery pulse approximates a systolic pressure of 80 to 90mm Hg).

Oxygen delivered by a mask at relatively high rate (6 to 10 L/min) is very important in the initial treatment of moderate and severe reactions to intravascular contrast media, and for those situations unrelated to contrast media that occur in the radiology department or angiography suite (e.g. vagal reaction, hypotension, cardiac ischaemia). Hypoxia can be a major complicating factor related to the above situations, and the effect of drugs used for treatment of reactions, especially epinephrine (adrenaline), can be affected adversely. A partial 'nonrebreather' mask is optimal; nasal 'prongs' are much less effective. Oxygen should be used for all patients; a history of chronic obstructive pulmonary disease or emphysema is not a contraindication to the institution of oxygen therapy for an acute reaction.

Intravascular fluid replacement is very important and it alone has been reported to be the most effective treatment for hypotension.[48] Early institution of intravenous fluid before starting drug therapy should be re-emphasised as highest priority in treating hypotension.

Epinephrine is an excellent, if not the best, drug for treating certain serious contrast reactions. The α-agonist effects of epinephrine reverse peripheral vasodilation and increases blood pressure. These vasoconstrictor changes decrease angioedema and urticaria. The β-agonist actions of epinephrine reverse bronchoconstriction, produce positive inotropic and chronotropic cardiac effects (increase in strength and rate of cardiac contractions), which also increase blood pressure, and may increase intracellular cyclic adenosine monophosphate (cAMP) levels.[49,50] Increments in baseline cAMP levels are generally considered to inhibit mediator release from inflammatory cells. It is absolutely essential that every radiologist who administers contrast material is comfortable using epinephrine.[51]

Epinephrine use demands careful attention and specific application. For example, in individuals with a fragile intracerebral or coronary circulation, the α-agonist effects of a large dose of epinephrine may invoke a hypertensive crisis that could produce a stroke or myocardial ischaemia.[52] β-Receptor sites ordinarily respond to lower doses of epinephrine than α-sites, but if a patient is taking β-blockers, the refractory response that may occur could encourage the radiologist to increase the dose of epinephrine to the point that unwanted α-effects would be generated. Patients with chronic asthma may simulate patients receiving β-blockers since a systemic β-adrenergic hyporesponsiveness has long been appreciated in this group of patients. When such patients develop an anaphylaxis-like reaction with asthmatic symptoms requiring β-receptor stimulation, one option is to treat with isoprenaline (isoproterenol) as the primary adrenergic drug, combined with more conservative doses of epinephrine.[53,54]

Epinephrine should be avoided, when possible, in treating the pregnant patient with a severe contrast media reaction and hypotension.[55] Because uterine vessels are sensitive, the α-effect of epinephrine, the combination of systemic hypotension plus vasoconstriction by epinephrine, can cause sequelae to the fetus. Ephedrine is suggested as an alternative medication.

Antihistamines and H_2 antagonists have limited therapeutic roles in treating contrast media reactions. They are used primarily to reduce symptoms from skin reactions. Antihistamines not effective for pruritus. The combination of antihistamines and H_2 antagonists is more effective for urticaria.

High dose intravenous corticosteroids do not play a significant role in the treatment of the acute situation; they may be effective in reducing delayed recurrent symptoms, which can be observed for as long as 48 hours after an initial reaction. It takes 4 to 6 hours before corticosteroids exhibit their activity.[37,56]

Inhaled β_2-adrenergic agonists such as salbutamol (albuterol), orciprenaline (metaproterenol) and terbutaline deliver large doses of bronchodilating β_2-agonist drugs directly to the airways with minimal systemic absorption and, therefore, minimal cardiovascular effects.

Atropine blocks vagal stimulation of the cardiac conduction system. Since low doses of atropine can be detrimental in treating bradycardia associ-

Table III. Treatment of specific reactions: nausea/vomiting

	Severity of nausea and vomiting	
	transient	severe, protracted
Treatment	Supportive	Injectable prochlorperazine
Adult dose/route		IM or IV 5-10mg
Childhood dose/route		>2-years-old: IM 0.13 mg/kg <2-years-old: not recommended
Treatment interval		Every 3-4h
Treatment precautions		IV administration should be slow

IM = intramuscular; **IV** = intravenous.

ated with contrast media–induced vagal reactions, larger doses are indicated.[51,57-60]

4.1 Treatment for Specific Reactions

4.1.1 Nausea and Vomiting

Nausea and vomiting, though usually self-limiting, may be the first signs of a more severe reaction. With urography using ionic high-osmolar contrast media, 15 to 20% of fatal reactions begin with nausea and vomiting.[61] For this reason, the patient should be observed closely for systemic symptoms, while maintaining intravenous access. The rate of injection should be slowed or stopped. In severe, protracted cases, injectable prochlorperazine may be used (table III).

4.1.2 Cutaneous Reactions

Treatment is usually not necessary for only a few scattered hives or pruritus. However, the patient should be observed closely for other developing systemic symptoms, while maintaining intravenous access. Only if the urticaria is extensive or bothersome to the patient should treatment be instituted (table IV).

4.1.3 Bronchospasm

Bronchospasm without coexisting cardiovascular problems should be treated with oxygen and inhaled bronchodilators (table V). Using a metered dose inhaler, treatment typically involves 2 to 3 deep inhalations. Epinephrine is indicated if bronchospasm is unrelieved by the inhaled bronchodilators.

4.1.4 Laryngeal Oedema

Laryngeal oedema does not respond well to inhaled β-agonists and, in fact, these agents may actually worsen laryngeal oedema. Therefore, clinical evaluation and auscultation of the patient prior to beginning treatment is extremely important to differentiate laryngeal oedema from bronchospasm. Epinephrine is the primary treatment for laryngeal oedema (table VI).

4.1.5 Hypotension

Profound hypotension may occur without respiratory symptoms. Normal sinus rhythm and tachy-

Table IV. Treatment of specific reactions: urticaria

	Severity of urticaria		
	scattered, transient	scattered, protracted	profound
Treatment	Supportive	Injectable diphenhydramine	Add: injectable cimetidine or injectable ranitidine Consider: epinephrine (adrenaline)
Adult dose/route		IV or IM 25-50mg	IV cimetidine 300mg (diluted in 20ml) IV ranitidine 50mg (diluted in 20ml) SC epinephrine 1 : 1000, 0.1-0.3ml (0.1-0.3mg) or IV epinephrine 1 : 10 000, 1ml (0.1mg) [repeat as needed]
Childhood dose/route		IV or IM 1.25 mg/kg	IV cimetidine 5-10 mg/kg (diluted) Ranitidine not recommended SC epinephrine 0.01 mg/kg up to a maximum dose of 0.3mg or IV epinephrine 0.01 mg/kg up to a maximum of 0.1mg [repeat as needed]
Treatment interval		Every 2-3h	Every 6-8h
Treatment precautions	Observe patient	Drowsiness, hypotension	Administer slowly

IM = intramuscular; **IV** = intravenous; **SC** = subcutaneous.

cardia differentiates this reaction from the so-called vagal reaction (hypotension plus sinus bradycardia). Initially, the patient's legs should be elevated since it returns about 700ml of blood to the central circulation.[49] Isolated hypotension is best treated initially by rapid intravenous fluid replacement rather than with vasopressor drugs (table VII). A total volume of up to 3L may be required to reverse the hypotension.

4.1.6 Vagal Reaction

A vagal reaction is characterised by the combination of prominent sinus bradycardia (pulse rate <60 beats/min) plus hypotension (systolic pressure <80mm Hg). Although its exact cause is unknown, the vagal reaction seems to be elicited or accentuated by anxiety. Proper recognition of this reaction and its bradycardia is absolutely vital to initiating the appropriate therapy of increasing intravascular fluid volume plus reversing the vagal stimulation. Elevation of the patient's legs and rapid infusion of intravenous fluids treats the vasodilation and expanded vascular space; the bradycardia is treated by intravenous administration of atropine to block vagal stimulation of the cardiac conduction system (table VII).

4.1.7 Anaphylactoid Reactions

These are acute, rapidly progressing, generalised systemic reactions characterised by multisystem involvement with pruritus, urticaria, angioedema, respiratory distress (bronchospasm and/or laryngeal oedema), and profound hypotension that requires prompt response. Initial treatment includes maintenance of airway, administration of oxygen, rapid infusion of intravenous fluids, and administration of adrenergic medications (table VIII). Epinephrine is the drug of choice and should be administered intravenously for rapid, effective action, and to avoid suboptimal absorption from subcutaneous tissues because of developing hypotension. A low dose [1.0ml (0.1mg) of 1 : 10 000 solution] is given at a relatively slow rate (over 2 to 5 minutes) and is titrated to effect.[51,52,60,62,63] If the reaction is not responding to this initial, slowly administered, low intravenous dose, increase the rate of injection. If there is no venous access, one should give epinephrine initially as a subcutaneous injection, using a larger dose, e.g. 0.3mg, and then try to establish venous access. In an emergency, epinephrine can be administered via the airway (inhaled, transtracheal, endotracheal).[49,54]

Table V. Treatment of specific reactions: bronchospasm

1. Oxygen by mask (6-10 L/min)
2. β_2-Agonist metered dose inhaler (2-3 deep inhalations)
3. Epinephrine (adrenaline):
Normal blood pressure, stable bronchospasm
Subcutaneous: 1 : 1000, 0.1-0.3ml (0.1-0.3mg) [use smaller dose in a patient with coronary artery disease or elderly patient]
In paediatric patients: 0.01 mg/kg up to a maximum dose of 0.3mg
Progressive bronchospasm and/or decreased blood pressure
Intravenously: 1 : 10 000, 1ml (0.1mg), slowly (e.g. over 2-5 min)
In paediatric patients: 0.01 mg/kg intravenously

Intravenous epinephrine should be given with caution to elderly patients. In the presence of hypoxia, there is increased risk of severe cardiac arrhythmias. Additionally, the amount of intravenous epinephrine should be limited in patients who are receiving noncardioselective β-blockers (e.g. propranolol). It should be avoided, if possible, in the pregnant patient experiencing an anaphylactoid reaction with hypotension. However, if the hypotension of the mother is not responding to conventional therapy (and ephedrine is not readily available), intravenous epinephrine may be necessary.

When the use of epinephrine is inadvisable, bronchospasm can be treated with a β_2-agonist inhaler (β_2 with no α-effects or β_1-effects). Alternatively, intravenous isoprenaline can be used in patients receiving noncardioselective β-blockers to 'over-ride' the β-blockade. The appropriate dosage can be titrated to effect starting with the 1 : 5000 solution diluted to 10ml and administered at 20

Table VI. Treatment of specific reactions: laryngeal oedema

1. Oxygen by mask (6-10 L/min)
2. Intravenous epinephrine (adrenaline): 1 : 10 000, 1ml (0.1mg) slowly over 2 to 5 min, repeat and/or increase rate of injection as needed

Table VII. Treatment of specific reactions: hypotension

Isolated hypotension
1. Elevate patient's legs
2. Oxygen by mask (6-10 L/min)
3. Intravenous fluid: rapid administration of sodium chloride 0.9% or lactated Ringer's solution
4. If unresponsive: vasopressor i.e. dopamine, norepinephrine (noradrenaline) or epinephrine (adrenaline) [e.g. epinephrine: 1 : 10 000, 1ml (0.1mg) given slowly over 2-5 min. Increase rate of injection as needed]
Vagal reaction (hypotension and bradycardia)
1. Elevate patient's legs
2. Oxygen by mask (6-10 L/min)
3. Intravenous fluids: rapid administration of sodium chloride 0.9%, or lactated Ringer's solution
4. Atropine 0.6-1.0mg intravenously, repeat if necessary after 3-5 min, to 3mg total (0.04 mg/kg) in adults. In paediatric patients give 0.02 mg/kg intravenously (up to a maximum of 0.6mg per dose); repeat if necessary to a total dose of 2mg

μg/min (1 ml/min). A small amount of intravenous 1 : 10 000 epinephrine is also given to the patient to achieve some α-effect (vasoconstriction) and thereby correct laryngeal oedema and angioedema. Another option for treatment of the patient taking β-blockers is glucagon, because of its positive inotropic and chronotropic effects on the heart.[64] The cardiac stimulant effects of glucagon are not associated with increased myocardial irritability, in contrast to isoprenaline. The dose of glucagon is 1 to 5mg by intravenous bolus, followed by an intravenous infusion of 5 to 15 μg/min. Both glucagon and isoprenaline may cause hypotension.

4.1.8 Contrast Medium Nephrotoxicity

The finding of increased serum creatinine levels and/or lack of urinary output within the first days following contrast medium administration, and no other reliable cause of the change in renal function, indicates contrast medium–induced nephrotoxicity. There is no specific treatment. Haemodialysis has been tried, but this should only be performed when there is clinical need. The patient should not be re-exposed to contrast media before the kidney function has returned to baseline. If contrast is to be given again, the patient must be adequately hydrated.

5. Conclusion

Prompt recognition and treatment can be invaluable in blunting an adverse response of a patient to radiographic contrast material and may prevent a reaction from becoming severe or even life-threatening. Radiologists and their staff should review treatment protocols regularly so that each can accomplish his or her role efficiently.[51,56,60,65,66] This is important in all radiology departments, but is even more important in radiology departments where only non-ionic low-osmolar contrast media

Table VIII. Treatment of specific reactions: generalised anaphylactoid reaction

1. Call for assistance
2. Suction airway as needed
3. Elevate patient's legs if hypotensive
4. Oxygen by mask (6-10 L/min)
5. Intravenous epinephrine (adrenaline): 1 : 10 000, 1 ml (0.1mg), given slowly over 2 to 5 min. Repeat as needed. If there is no venous access, give the first dose subcutaneously. In paediatric patients use 0.01 mg/kg to a maximum dose of 0.1mg
6. Intravenous fluids (e.g. sodium chloride 0.9%, lactated Ringer's solution)
7. Histamine H_1 blocker e.g. diphenhydramine 25-50mg intravenously
8. β_2-Agonist metered dose inhaler for persistent bronchospasm: 2 or 3 inhalations
9. Adrenergic options for patients taking β-blockers: glucagon: (1-5mg intravenously as a bolus followed by infusion of 5-15 μg/min); isoprenaline (isoproterenol): 1 : 5000 solution for injection (0.2 mg/ml) intravenously, 0.5-1.0ml diluted to 10ml with sodium chloride 0.9%, 1ml (20μg) increments

are used, since adverse events are more rarely seen at such departments. Knowledge, training and preparation are crucial in guaranteeing appropriate and effective therapy in the event of an adverse contrast-related event.

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